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(54) Resurfacing of rodent antibodies

Oberflächenumformung von rodenten Antikörpern Remodelage d'anticorps des rongeurs

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 MOLECULAR IMMUNOLOGY vol. 28, no. 4/5, 1991, GB pages 489 - 498 PADLAN A E
 'POSSIBLE PROCEDURE FOR REDUCING THE IMMUNOGENICITY OF ANTIBODY VARIABLE DOMAINS WHILE PRESERVING THEIR LIGAND-BINDING PROPERTIES'

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Description

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FIELD OF THE INVENTION

[0001] The present invention relates to the development of prediction rules that can be used to accurately model the variable regions (V-regions) of antibodies. The development of these rules and their application in the predictive molecular restructuring of the surfaces of variable domains of non-human monoclonal antibodies enables changing of the surface, i.e., resurfacing, of these monoclonal antibody V-regions to replicate the surface characteristics found on human antibody V-regions. This method of resurfacing non-human monoclonal antibody V-regions to resemble human antibody V-regions is expected to permit the production of functional altered antibodies, which retain the binding parameters of the original non-human monoclonal antibody, with improved therapeutic efficacy in patients due to the presentation of a human surface on the V-region.

BACKGROUND OF THE INVENTION

General Background of Antibodies

[0002] Murine monoclonal antibodies are widely used as diagnostic and therapeutic agents in the treatment of human disease. Mice can be readily immunized with foreign antigens to produce a broad spectrum of high affinity antibodies. Invariably, the introduction of murine or other rodent antibodies into humans results in the production of a human antimouse antibody (HAMA) response due to the presentation of a foreign protein in the body. The production of HAMA in patients can result from the introduction of foreign antibody in a single dose or from extended use in therapy, for example, for the treatment of cancer. Extended use of murine antibody is generally limited to a term of days or weeks in patients before concerns of anaphylaxis arise. Moreover, once HAMA has developed in a patient, future use of murine antibodies for diagnostic or therapeutic purposes is often precluded for the same reasons.

[0003] Beyond ethical considerations, attempts to produce human monoclonal antibodies have not been highly successful for a number of reasons. The production *in vitro* of human monoclonals rarely results in high affinity antibodies. *In vitro* cultures of human lymphocytes yield a restricted range of antibody responses relative to the broad spectrum of reactive antibodies produced *in vivo* through direct immunization of mice. Additionally, in humans, immune tolerance prevents the successful generation of antibodies to self-antigens. All of these factors have contributed to the search for ways to modify the structures of murine monoclonal antibodies to improve their use in patients. Many investigators have attempted to alter, reshape or humanize murine monoclonal antibodies in an effort to improve the therapeutic application of these molecules in patients.

35 Strategies of Antibody Humanization

[0004] The earliest reports of the controlled rearrangement of antibody domains to create novel proteins was demonstrated using rabbit and human antibodies as described by Bobrzecka, K. et al. (Bobrzecka, K., Konieczny, L., Laidler, P. and Rybarska, J. (1980), Immunology Letters 2, pp. 151-155) and by Konieczny et al. (Konieczny, L., Bobrzecka, K., Laidler, P. and Rybarska, J. (1981), Haematologia 14 (I), pp. 95-99). In those reports, the protein subunits of antibodies, rabbit Fab fragments and human Fc fragments, were joined through protein disulfide bonds to form new, artificial protein molecules or chimenc antibodies.

[0005] Recombinant DNA technology was used to construct gene fusions between DNA sequences encoding mouse antibody variable light and heavy chain domains and human antibody light chain (LC) and heavy chain (HC) constant domains to permit expression of the first recombinant "near-human" antibody (chimeric antibody) product (Morrison, S.L., Johnson, M.J., Herzenberg, L.A. and Oi, V.T. (1984), Proc. Natl. Acad. Sci. U.S.A. 81, pp. 6851-6855).

[0006] The kinetics and immune response in man to chimeric antibodies has been examined (LoBuglio, A.F., Wheeler, R.H., Trang, J., Haynes, A., Rogers, K., Harvey, E.B., Sun, L., Ghrayeb, J. and Khazaeli, M.B. (1989), Proc. Natl. Acad. Sci. 86, pp. 4220-4224).

[0007] Chimeric antibodies contain a large number of non-human amino acid sequences and are immunogenic in man. The result is the production of human anti-chimera antibodies (HACA) in patients. HACA is directed against the murine V-region and can also be directed against the novel V-region/C-region (constant region) junctions present in recombinant chimeric antibodies.

[0008] To overcome some of the limitations presented by the immunogenicity of chimeric antibodies, the DNA sequences encoding the antigen binding portions or complementarity determining regions (CDR's) of murine monoclonal antibodies have been grafted by molecular means in the DNA sequences encoding the frameworks of human antibody heavy and light chains (Jones, P.T., Dear, P.H., Foote, J., Neuberger, M.S. and Winter, G. (1986), Nature 321, pp. 522-525; Riechmann, L., Clark, M., Waldmann, H. and Winter, G. (1988), Nature 332, pp. 323-327). The expressed

recombinant products called reshaped or humanized antibodies are comprised of the framework of a human antibody light or heavy chain and the antigen recognition portions, CDR's, of a murine monoclonal antibody. Several patent applications have been filed in this area including, for example, European Patent Application, Publication No. 0239400; European Patent Application, Publication Nos. 0438310A1 and 0438310A2; International Patent Publication No. WO 91/09967; and International Patent Publication No. WO 90/07861.

[0009] However, it is questionable whether European Patent Application (EP), Publication No. 0239400 is truly enabling. It is not assured in this patent that the best fit is made to assure proper presentation of the CDR loops at the antibody combining site.

[0010] EP Publication Nos. 0438310A1 and 0438310A2 go a step beyond EP Publication No. 0239400 by protecting the importance of uniquely selected human frameworks for the human light chain (LC) and heavy chain (HC) V-regions. These V-region frameworks should show a high degree of sequence similarity with the frameworks of the murine monoclonal antibody and present the CDR's in the appropriate configuration. However, the criteria for sequence matching are no more sophisticated than simple homology searching of the antibody protein or DNA databases.

[0011] International Patent Publication No. WO 91/09967 attempts a further variation of the method disclosed in EP Publication No. 0239400. In International Patent Publication No. WO 91/09967, homology of the donor sequences and the acceptor framework is not important, rather it discloses that a selected set of residues in the LC and HC are critically important to humanization. The ability to make changes at these positions is the basis of International Patent Publication No. WO 91/09967.

[0012] International Patent Publication No. WO 90/07861 proposes four important criteria for designing humanized antibodies. 1) Homology between human acceptor and non-human donor sequences. 2) Use donor rather than acceptor amino acids where the acceptor amino acid is unusual at that position. 3) Use donor framework amino acids at positions adjacent to the CDR. 4) Use donor amino acids at framework positions where the sidechain atom is within 3 x 10⁻¹⁰ (3 Angstroms) of the CDR in a 3-D model. The first antibody humanized by this method retained less than 1/3 the affinity of the original monoclonal antibody.

[0013] None of the above methods for designing a humanized antibody are predictable due to the questions that surround CDR framework interactions. By replacement of murine framework with human framework, there is no guarantee of identical conformations for CDR's because i) the V_L-V_H interaction is not identical in all V-regions and ii) accurate prediction of the CDR-framework interactions are key to faithful reproduction of the antigen binding contacts. [0014] The above methods do not offer a general solution to solving the issues surrounding antibody humanization, rather the methods as outlined in each reference above involve a substantial amount of trial and error searching to obtain the desired affinity in the final humanized product. More importantly, there is no guarantee that corrective changes in framework amino acids will leave the reshaped V-regions resembling the surface character of a truly human antibody. Therefore, it can be argued that antibodies humanized by the above methods may be immunogenic in man.

35 Antigenicity of Antibodies

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[0015] The antigenicity/immunogenicity of an antibody, including recombinant reshaped antibody products, introduced into humans can be viewed as a surface phenomenon. In general one can view the immune system as scanning the surface of a protein introduced to the body. If the F_v portion of a humanized antibody 'opens-up' in the circulation then internal residues can be presented to the immune system. On the other hand, if the F_v portion is stable and tightly packed then only the surface residues presented by the V-regions and the interface between the V_L and V_H regions will be 'scanned'.

Surface Reshaping or Resurfacing of Antibodies

[0016] The notion of surface presentation of proteins to the immune system raises the prospect of redesigning murine monoclonal antibodies to resemble human antibodies by humanizing only those amino acids that are accessible at the surface of the V-regions of the recombinant F_v. The resurfacing of murine monoclonal antibodies to reduce their immunogenicity could be beneficial in maintaining the avidity of the original monoclonal antibody in the reshaped version, because the natural framework-CDR interactions are retained. The value of maintaining the integrity of the framework-CDR interactions has been illustrated as summarized below.

[0017] In a recent research report, two different reshaped versions of the rat monodonal antibody, Campath-9 (antihuman CD4), were generated (Gorman, S.D., Clark, M.R., Routledge, E.G., Cobbold, S.P. and Waldmann, H. (1991), Proc. Natl. Acad. Sci. U.S.A. 88, pp. 4181-4185). In one version, pV_HNEW/C_{G1}, the acceptor V_H framework was from the human NEW-based heavy chain, which has 47% identical residues to the Campath-9 V_H. While in the second version, pV_HKOL/C_{G1}, the acceptor V_H framework was from the human KOL antibody, which has 72% identical residues to Campath-9 V_H. Each reshaped antibody contained the identical V_L domain from the human REI antibody sequence. However, the recombinant product of pV_HKOL/C_{G1} had an avidity for CD4 that was substantially greater than the

product of pV_HNEW/C_{G1}. The authors proposed a reshaping strategy where human sequences, that are highly homologous to the rodent antibody of interest, are transferred, by in vitro mutagenesis, into the rodent V-region to create a "bestfit" reshaped antibody. This strategy uses the term "bestfit" to describe the modeling process, however, there is no quantitative formula employed to assess "bestfit", and so in effect, the process is subjective. Additionally, there is no resurfacing concept presented in that paper.

[0018] The concept of reducing rodent-derived antibody immunogenicity through the replacement of exposed residues in the antibody framework regions which differ from those of human origin is discussed in a recent paper (Padlan, E.A. (1991), Molecular Immunology 28, pp. 489-498). In that paper, the variable domains of two antibody structures, KOL (human) and J539 (mouse), are examined. The crystal structures of the Fab fragments of these two antibodies have been elucidated to high resolution. The solvent accessibility of the exposed framework residues in the variable domains of these two antibodies were compared to a sequence database of human and murine antibody V-region subgroups. On the basis of his findings, Padlan proposed to reduce the antigenicity of allogeneic variable domains [murine V-regions], through replacement of the exposed residues in the framework regions with residues usually found in human antibodies. In murine sequences with the highest similarity to a given human sequence, the number of changes necessary to "humanize" a murine V-region surface would range from 6-15 amino acid changes per V-region. This reference suggests how to convert one antibody surface into another but no general method is developed. Application of the procedure is provided by two examples, a worst-case and a best-case.

Worst Case:

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[0019] Among the representative murine kappa V_L sequences examined for which its autologous V_H has been sequenced, S107 V_L has the most residues that need to be replaced to humanize it. S107 V_L is most similar to the members of the human subgroup VKIV and JK2. The exposed or partially exposed residues that need to be replaced are those at positions $\underline{9}$, 10, 14, $\underline{15}$, 16, 17, 18, $\underline{22}$, $\underline{41}$, $\underline{63}$, 80, $\underline{83}$, $\underline{85}$, 100 and 106. Murine V-region S107 V_H is most similar in its framework to the members of the human subgroup VHIII and JH6. The exposed or partially exposed residues in S107 V_H that need to be replaced are those at positions 3, 40, 68, 73, 75, 76, 82b and 89. A total of 23 residues need to be replaced to humanize the variable domains of S107.

Best Case:

[0020] Among the murine V_H sequences examined for which the autologous V_L has also been sequenced, MOPC21 V_H has the least number of residues that need to be replaced to humanize it. MOPC21 V_H is most similar in its framework to the members of the human subgroup HIII and JH6. The exposed or partially exposed residues that need to be replaced are those at positions 1, 42, 74, 82a, 84, 89 and 108. MOPC21 V_L is most similar in its framework to human subgroup VKIV and JK4. The exposed or partially exposed residues that need to be replaced are those at positions 1, 9, 12, 15, 22, 41, 63, 68, 83 and 85. A total of 17 amino acids need to be replaced to humanize the variable domains of MOPC21.

[0021] Of the light chains in the Best- and Worst-Case examples cited above, S107V_L required changes at 15 positions and MOPC21V_L required changes at 10 positions. Only seven of the changes are common to both of these light chain sequences (see underlined residues). Moreover, of the heavy chain residues that need to be replaced to humanize the respective V-regions, S107V_H required changes at 8 positions and MOPC21V_H required changes at 7 positions. In this instance, only one position is common to both of these heavy chain sequences (see residues in boldface).

[0022] An analysis of S107 V-regions alone would not have led to the prediction of which residues to change in MOPC21. The reason for this is that the surface residues in Padlan's analysis are only determined by reference to the crystal structure analysis of <u>one</u> antibody. In addition, the basis for defining the surface exposure of an amino acid at a particular position on that crystal structure is a continuous gradient of change, e.g., the fractional solvent accessibility values (Padlan, E.A. (1990), Molecular Immunology 28, pp. 489-498) were computed, where: 0 to 0.2 = completely buried, 0.2 to 0.4 = mostly buried, 0.4 to 0.6 = partly buried/partly exposed, 0.6 to 0.8 = mostly exposed, and 0.8 or above = completely exposed. By limiting the analysis of exposed surface residues to a single crystal structure and by superimposing a broad range of solvent accessibility ratios on exposed residues, such a modeling strategy could be expected to have a wide margin of error in its calculations. This model fails to take into account the great majority of structural information available in the database for other antibody crystal structures.

SUMMARY OF THE INVENTION

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[0023] Accordingly, it is an object of this invention to provide humanized rodent antibodies or fragments thereof, and in particular, humanized rodent monoclonal antibodies that have improved therapeutic efficacy in patients due to the presentation of a human surface on the V-region. This and other objects have been attained by providing a method of

producing paired peptides which may or may not be covalently bonded via a disulfide bond or peptide linker, and which comprise humanized heavy and light chains of a rodent antibody variable region, said method comprising:

- (a) generating sequence alignments, in framework positions only, from relative accessibility distributions from x-ray crystallographic structures of a pool of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions;
- (b) defining for a rodent antibody variable region a set of heavy and light chain surface exposed amino acid residues using said set of surface exposed framework positions generated in said step (a);
- (c) identifying from human antibody amino acid sequences a set of variable region heavy and light chain surface exposed amino acid residues that is most closely identical to said set of rodent surface exposed amino acid residues defined in said step (b), wherein said heavy and light chains from said human antibody are or are not naturally paired;
- (d) substituting, in the amino acid sequence of said rodent variable region, said set of heavy and light chain surface exposed amino acid residues defined in said step (b) with said human set of heavy and light chain surface exposed amino acid residues identified in said step (c);
- (e) constructing three-dimensional models of said variable region of said rodent antibody and of said variable region of said rodent antibody resulting from the substituting specified in said step (d);
- (f) comparing said three-dimensional models constructed in said step (e) and identifying any amino acid residues from said sets identified in said steps (b) and (c) that are close to any atom of any residue of the complementarity determining regions of said rodent variable region;
- (g) changing any residues identified in said step (f) from the human to the original rodent amino acid residue to thereby define a humanizing set of surface exposed amino acid residues;
- (h) replacing the set of rodent antibody variable region surface exposed amino acid residues defined in said step
- (b) with the humanizing set of surface exposed amino acid residues defined in said step (g); and
- (i) producing said paired peptides,

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wherein in step (a) sequence alignments are generated from a sufficient number of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions wherein said set is identical in at least about 98% of said sequence alignment positions and in that in step (f) amino acid residues from said sets identified in said steps (b) and (c) that are within 5x10⁻¹⁰m (5 Ångstroms) of any atom of any residue of the complementarity determining regions of said variable region to be humanized are identified.

[0024] Also provided is a method of producing a humanized rodent antibody or fragment thereof by resurfacing, said method comprising:

- (a) generating sequence alignments, in framework positions only, from relative accessibility distributions from x-ray crystallographic structures of a pool of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions;
 - (b) defining for a rodent antibody or fragment thereof a set of variable region heavy and light chain surface exposed amino acid residues using said set of surface exposed framework positions generated in said step (a);
 - (c) identifying from human antibody amino acid sequences a set of variable region heavy and light chain surface exposed amino acid residues that is most closely identical to said set of rodent surface exposed amino acid residues defined in said step (b), wherein said heavy and light chains from said human antibody are or are not naturally paired;
 - (d) substituting, in the amino acid sequence of said rodent antibody or fragment thereof, said set of heavy and light chain surface exposed amino acid residues defined in said step (b) with said human set of heavy and light chain surface exposed amino acid residues identified in said step (c);
 - (e) constructing three-dimensional models of said variable region of said rodent antibody or fragment thereof and of said variable region of said rodent antibody or fragment thereof resulting from the substituting specified in said step (d):
- (f) comparing said three-dimensional models constructed in said step (e) and identifying any amino acid residues from said sets identified in said steps (b) and (c) that are close to any atom of any residue of the complementarity determining regions of said rodent antibody or fragment thereof;
 - (g) changing any residues identified in said step (f) from the human to the original rodent amino acid residue to thereby define a humanizing set of surface exposed amino acid residues;
 - (h) replacing the set of rodent antibody surface exposed amino acid residues defined in said step (b) with the humanizing set of surface exposed amino acid residues defined in said step (g); and
 - (i) producing said humanized antibody or fragment thereof;

wherein in step (a) sequence alignments are generated from a sufficient number of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions wherein said set is identical in at least about 98% of said sequence alignment positions and in that in step (f) amino acid residues from said sets identified in said steps (b) and (c) that are within 5x10⁻¹⁰m (5 Ångstroms) of any atom of any residue of the complementarity determining regions of said rodent antibody or fragment thereof to be humanized are identified.

[0025] In a preferred embodiment, the rodent antibody or fragment thereof is a murine antibody, and most preferably murine antibody N901.

BRIEF DESCRIPTION OF THE FIGURES

[0026]

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Figure 1 shows an algorithm that can be used for constructing a three-dimenensional model of the rodent antibody variable region.

Figure 2 is a diagram showing the approach to determine how to humanize a rodent antibody or fragment thereof according to the present invention.

Figures 3A and 3B are plots of relative accessibility of amino acid residues for twelve antibody F_v structures, mapped onto the sequence alignment of these structures. Structures Glb2 (Jeffrey, P.D., Doctor of Philosophy Thesis, University of Oxford, United Kingdom, 1991), D1.3 (Amit, A.G., Mariuzza, R.A., Phillips, S.E.V. and Poljak, R.J. (1986), Science 233, pp. 747-753), 3D6 (Grunow, R., Jahn, S., Porstman, T., Kiessig, T., Steinkeller, H., Steindl, F., Mattanovich, D., Gurtler, L., Deinhardt, F., Katinger, H. and von R., B. (1988), J. Immunol. Meth. 106, pp. 257-265) and 36-71 (5fab) (Rose, D.R., Strong, R.K., Margolis, M.N., Gefter, M.L. and Petsko, G.A. (1990), Proc. Natl. Acad. Sci. U.S.A. 87, pp. 338-342) are not yet present in the Brookhaven database. The other structures used were: 2hfl (Sheriff, S., Silverton, E.W., Padlan, E.A., Cohen, G.H., Smith-Gill, S.J., Finzel, B.C. and Davies, D.R. (1987), Proc. Natl. Acad. Sci. U.S.A. 84, pp. 8075-8079), 3hfm (Padlan, E., Silverton, E., Sheriff, S., Cohen, G., Smith-Gill, S. and Davies, D. (1989), Proc. Natl. Acad. Sci. U.S.A. 86, pp. 5938-5942), 2fbj (Mainhart, C.R., Potter, M. and Feldmann, R.J. (1984), Mol. Immunol. 21, pp. 469-478), 3fab (Saul, F.A., Amzel, L.M. and Poljak, R.J. (1978), J. Biol. Chem. 253, pp. 585-597), 4fab (Herron, J., He, X., Mason, M., Voss, E. and Edmunson, A. (1989), Proteins: Struct., Funct., Genet. 5, pp. 271-280), 2mcp (Segal, D., Padlan, E., Cohen, G., Rudikoff, S., Potter, M. and Davies, D. (1974), Proc. Natl. Acad. Sci. U.S.A. 71, pp. 4298), 2fb4 (Marquart, M. Deisenhofer, J. and Huber, R. (1980), J. Mol. Biol. 141, pp. 369-391), and 1f19 (Lascombe, M. Alzari, P., Boulot, G., Salujian, P., Tougard, P., Berek, C., Haba, S., Rosen, E., Nisonof, A. and Poljak, R. (1989), Proc. Natl. Acad. Sci. U.S.A. 86, p. 607). These structures are designated by their Brookhaven entry code. The sequence numbering used here is described in Figures 4A and 4B. Figure 3A graphically shows the relative accessibility for the heavy chain and Figure 3B graphically shows the relative accessibility for the light chain.

Figures 4A and 4B show alignments of sequences generated using the three methods of humanization. Sequences are: 1) Original rodent N901. 2+3) KOL (Marquart, M. Deisenhofer, J. and Huber, R. (1980), J. Mol. Biol. 141, pp. 369-391) and reshaped N901 using KOL surface. 4+5) Most homologous sequences, L(KV2F) (Klobeck, H., Meindl, A., Combriato, G., Solomon, A. and Zachau, H. (1985), Nucleic Acids Res. pp. 6499-6513) and H(G36005) (Schroeder, H. and Wang, J. (1990), Proc. Natl. Acad. Sci. U.S.A. 87), and reshaped N901 using these sequences. 6+7) Most homologous with respect to surface residues, L(KV4B) (Klobeck, H., Bronkamp, G., Combriato, G., Mocikat, R., Pohelnz, H. and Zachau, H. (1985), Nucleic Acids Res. 3, pp. 6515-6529) and H(PLO123) (Bird, J., Galili, N., Link, M., Sites, D. and Sklar, J. (1988), J. Exp. Med. 168, pp. 229-245), and reshaped N901 using these sequences. The numbering is the same as used in the antibody modelling program ABM (trademark for commercial software, Oxford Molecular Ltd., Oxford, U.K.), which is based on structural conservation and not sequence homology as used by Padlan et al. (Kabat, E.A., Wu, T.T., Reid-Miller, M., Perry, H.M. and Gottesman, K.S. (1987), Sequences of Proteins of Immunological Interest. U.S. Department of Health and Human Services, Fourth Edition). The sequence changes which have to be introduced in order to resurface N901 with a given sequence are marked with bars, back-mutations as determined from F_v models are marked with stars. The sequence homology of given sequences to N901 are shown in brackets after each sequence.

Figure 5 is a stereo plot of mean antibody β -barrel, coordinates determined by iterative multiple fitting of eight antibody structures. Strands 7 and 8 comprise the 'take off' positions for CDR H3 and are not included in the fitting of V_L and V_H regions.

Figure 6 is a plot of RMS deviation from the mean of the eight β -sheet strands comprising the framework. The RMS was calculated from structures F19.9, 4-4-20, NEW, FBJ, KOL, HyHEL-5, HyHEL-10 and McPC603. N,C α , C atoms are included in the plot. The residues used are shown in the alignment (Table 2). The most disordered residues are all the residues of strand HFR4, the last residue of LFR1, and the first and last residue of HFR2. The nomenclature of the strands is explained in the alignment in Table 2. LFR1 - #1, LFR2 - #2, LFR3 - #3, LFR4 - #4,

HFR1 - #5, HFR2 - #6, HFR3 - #7, HFRS4 - #8.

Figure 7 is a flowchart of the overall modelling protocol known as CAMAL.

Figure 8 is a plot of superimposed loop backbones for models and x-ray structures discussed in Example 2. The loops are positioned after global framework fit. This does not represent the best local least squares fit, but shows how the loops are positioned globally onto the framework.

Figures 9A to 9D are stereo (N,C- α ,C,O) representations of crystal structures and models of D1.3, 3671 and Gloop-2 variable domain and β -barrel strands described in Example 2. Crystal structures are shown with open bonds, model with solid bonds. The difference between the 3D6-H3 in the model and the crystal structure is due to a 5-7° twist in the extended β -sheet conformation of this loop, Figure 9A: D1.3, Figure 9B: 36-71, Figure 9C: Gloop-2, Figure 9D: 3D6.

Figure 10 is a histogram showing the distribution of loop length for CDR H3 loops, data from Kabat et al. (Kabat, E.A., Wu, T.T., Reid-Miller, M., Perry, H.M. and Gottesman, K.S. (1987), Sequences of Proteins of Immunological Interest. U.S. Department of Health and Human Services, Fourth Edition).

15 DETAILED DESCRIPTION OF THE INVENTION

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[0027] The existence of specific, yet different, surface patches in murine and human antibodies may be the origin of the inherited immunogenicity of murine antibodies in humans. Statistical analysis of a database of unique human and murine antibody F_v fragments has revealed that certain combinations of residues in exposed surface positions are specific for human and murine sequences. The combinations are not the same in human and murine F_v domains. However, it is possible to define families of surface residues for the two species of antibodies. These families reveal a novel method for the "humanization" or reshaping of murine antibodies. Humanization is the modification of the solvent accessible surface of a non-human antibody or fragment thereof to resemble the surface of a chosen human antibody or fragment thereof such that the modified non-human antibody or fragment thereof exhibits lower immunogenicity when administered to humans. Such a process applies in the present application to antibody variable regions but could equally well apply to any other antibody fragment. The method is considered to be generally applicable to humanization of rodent antibodies.

[0028] According to the present invention, a statistical analysis is presented which is based on accessibility calculated for a range of antibody crystal structures. When this information is applied to an antibody sequence database, it is possible to discriminate between human and murine antibodies at the sequence level purely on the basis of their surface residue profiles.

Rational Resurfacing Approach

- 35 [0029] There are several key features of the resurfacing approach of the present invention.
 - 1) This method uses as a starting point, construction of a three-dimensional model of a rodent variable region by known methods:
 - 2) A large number (e.g., twelve) of antibody F_v or Fab fragment x-ray crystallographic structures are analyzed to produce an unambiguous set of surface exposed amino acid residues that will be positionally identical for a majority (98%) of antibodies. The set is produced by identifying all those residues whose solvent accessibility is above a given cut-off (typically 30%), calculated using a modification of the method of Kabsch and Sander (Kabsch, W. and Sander, C. (1983), Biopolymers 22, pp. 2257-2637) in which explicit atomic radii are used for each atom type to predict sidechain positions as is described below in more detail;
 - 3) Using a complete human antibody database, the best set of human heavy and light chain surface exposed amino acid residues is selected on the basis of their closest identity to the set of surface amino acid residues of the murine antibody;
 - 4) In order to retain the conformational structure of the CDRs of the rodent antibody, replacement of any human surface exposed amino acid with the original rodent surface exposed amino acid residue is carried out whenever a surface residue is calculated from the three-dimensional model to be within 5 Angstroms of a CDR residue.

[0030] The general resurfacing approach of the present invention is illustrated in Figure 2. The approach can be divided into two stages. In the first, the rodent framework (white) is retained and only the surface residues changed from rodent (dark grey circles) to the closest human pattern (light grey circles). This should remove the antigenicity of the rodent antibody. In the second stage, surface residues within 5x10⁻¹⁰m (5 Angstroms) of the CDRs are replaced with the rodent equivalents in an attempt to retain antigen binding and CDR conformation.

[0031] The method of the present invention is applicable to whole antibodies as well as antibody fragments. Suitable antibody fragments that can be used can readily be determined by the skilled artisan. Examples of some suitable

fragments include a single chain antibody (SCA), an antibody F_v fragment, Fab fragment, Fab₂ fragment, Fab' fragment, or other portion of an antibody comprising the binding site thereof.

[0032] According to the present invention, an important step in the method for determining how to modify a rodent antibody or fragment thereof by resurfacing is to determine the conformational structure of the variable region of the rodent antibody or fragment thereof to be humanized by constructing a three-dimensional model of the rodent antibody variable region. This can be done by known methods such as those described, for example, in Martin et al. (Martin, A. C.R., Cheetham, J.C. and Rees, A.R. (1989), Proc. Natl. Acad. Sci. U.S.A. 86, pp. 9268-9272; Methods in Enzymology (1991), 203, pp. 121-152) and as described in detail in Example 2.

[0033] Martin et al. describe an algorithm which is depicted in Figure 1. The algorithm applies to murine and human antibodies equally well. The present inventors therefore expect that, based on sequence similarity between antibodies of different species (Kabat, E.A. Segments of Proteins of Immunological Interest, National Institutes of Health, U.S.A. 1991), the algorithm will work equally well for rat and other rodent antibodies.

[0034] Briefly, the algorithm depicted in Figure 1 can be summarized as follows. The framework region of an antibody to be modelled is selected on the basis of sequence homology and constructed by a least squares fit onto the six conserved strands of the variable region β-barrel. Light and heavy chain complementarity determining regions are constructed using a combination of canonical structures (Chothia, C. and Lesk, A.M. (1987), J. Molec. Bio. 196, pp. 901-917), database searching and conformational searching. Detailed descriptions of these methods are described in Example 2 herein and in the above two references (Martin et al. 1989 and 1991).

[0035] According to the present invention, another three-dimensional model is also constructed. The other three-dimensional model is of the rodent antibody variable region having human antibody surface amino acid residues substituted therein at particular rodent antibody surface residue positions.

[0036] This other three-dimensional model is constructed by carrying out the series of steps described next.

[0037] The first of the steps is to generate sequence alignments from relative accessibility distributions from x-ray crystallographic structures of a sufficient number of antibody variable region heavy and light chains to give a set of framework positions of surface exposed amino acid residues which is identical in a majority (98%) of the variable regions.

[0038] As used herein, the term "framework" means the antibody variable region from which the complementarity determining regions have been excluded.

[0039] "Complementarity determining regions" means those amino acid sequences corresponding to the following numbering system as defined by Kabat, E.A. (In Sequences of Immunological Interest, N.I.H., U.S.A., 1991).

Light Chain residues L1 24-34 **Light Chain** L2 residues Light Chain L3 residues 89-97 Heavy Chain H1 residues 31-358 50-58 **Heavy Chain** H2 residues residues 95-102 **Heavy Chain** нз

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[0040] A sufficient number of rodent antibody fragments that need to be analyzed in order to produce the set of framework positions of surface exposed amino acid residues can readily be determined by the skilled artisan through routine experimentation using a database of antibody sequences. Thus, this step can be conducted using suitable databases now in existence or later compiled.

[0041] The x-ray crystallographic structures are used to determine relative accessibility distributions of surface exposed amino acid residues. The relative accessibility distributions identify all those residues whose solvent accessibility is above a given cut-off (typically 30%), calculated using a modification of the method of Kabsch and Sander (Kabsch, W. and Sander C. (1983), Biopolymers 22, pp. 2257-2637) in which explicit atomic radii are used for each atom type.

[0042] The relative accessibility distributions determined from the x-ray crystallographic structures can then be used to generate sequence alignments which give a set of framework positions of surface exposed amino acid residues which is identical in a majority (98%) of the variable regions.

[0043] The set of framework positions of surface exposed amino acid residues for the variable regions of murine antibodies is shown in Table 1, set forth in Example 1, and was produced using the sequence alignments and accessibility distributions shown in Figures 3A and 3B.

[0044] Once a set of framework positions of surface exposed amino acid residues for the variable regions of the rodent antibodies have been generated, the surface exposed residues of the heavy and light chain pair of the rodent antibody, or fragment thereof, to be humanized can be identified using an alignment procedure such as that described in Example 1 and shown in Figures 3A and 3B. This defines a set of surface exposed amino acid residues of a heavy and light chain pair of a rodent antibody or antibody fragment to be humanized.

[0045] Next, a complete human antibody sequence database is used to identify a set of surface exposed amino acid residues from a human antibody variable region that have the closest positional identity to the set of surface exposed amino acid residues of the variable region of the rodent antibody that is to be humanized. The set of surface exposed

amino acid residues from the human antibodies can be separately identified for a heavy chain and for a light chain that are not naturally paired and/or a set can be identified from a natural human heavy and light chain pair, that is, a pair originating from a single B cell or hybridoma clone. Preferably, the set is one from a natural human heavy and light chain pair.

[0046] A humanized rodent antibody that gives the appearance of a human antibody is then predicted by substituting the set of surface exposed amino acid residues from the rodent antibody or fragment thereof to be humanized with the set of surface exposed amino acid residues from the human antibody.

[0047] A three-dimensional model can then be constructed from the resulting, fully substituted variable region of the rodent antibody or fragment thereof. The three-dimensional model is constructed using the same known methods mentioned above for constructing a 3-D model of the original rodent antibody or fragment thereof.

[0048] While the antigenicity of this fully "resurfaced" or humanized antibody should be removed, an additional factor to be addressed is the binding affinity or the binding strength of the resurfaced antibody. Changes in the framework of the variable domain introduced through resurfacing can influence the conformation of the CDR loops and therefore antigen binding of the antibody. According to the present invention, this problem is removed by the next step which is to identify, by means of a comparison of both of the above-described three-dimensional models of the rodent antibody variable region, any residues from the set of surface exposed amino acid residues of the variable region heavy and light chain pair of the human antibody identified that are within 5 Angstroms of any atom of any residue of the rodent antibody or antibody fragment complementarity determining regions (CDRs).

[0049] Any residue(s) so identified is then changed back from the human to the original rodent amino acid residue(s). [0050] The results of this method can then be applied to a particular rodent antibody by well known methods. Briefly, genes for the humanized variable heavy and light chain regions are constructed using standard recombinant DNA methods (Sambrook, J., Fritsch, E.F. and Maniatis, T. (1989), Molecular Cloning, Second Edition). For example, a PCR method can be used (Daugherty et al. (1991), Nucleic Acids Research 19, pp. 2471-2476).

[0051] Variable heavy chain or variable light chain gene constructs are subcloned into appropriate expression vectors. Suitable expression vectors contain either a human gamma or human kappa constant region gene, a suitable promoter, a sequence coding for a human immunoglobulin leader peptide (for example: met-gly-trp-ser-cys-ile-ile-leu-phe-leu-val-ala-thr-ala-thr (SEQ ID NO:39), Olandi et al. (1989), PNAS 86, pp. 3833-3837), and a drug selectable marker.

[0052] Heavy and light chain expression plasmids can be co-transfected, for example, by electroporation into suitable cells, for example, SP2/0 cells, and selected with an appropriate drug, G418, for example. Screening for intact antibody can be accomplished by ELISA assay. 96-well plates are coated with, for example, goat anti-human kappa chain antibody, and light chains are detected with, for example, goat anti-human antibody conjugated to alkaline phosphatase. [0053] As another approach, light chain constructs are transfected, for example, by electroporation into suitable cells, for example, SP2/0 cells and selected, for example, in hygromycin. Screening for light chain expression can be accomplished by ELISA assay. 96-well plates are coated with, for example, goat anti-human kappa chain antibody, and light chains are detected with, for example, goat anti-human antibody conjugated to alkaline phosphatase.

[0054] A light chain producing line is then used as a host to electroporate in the heavy chain construct. The heavy chain plasmid is co-transfected with a plasmid containing the gene coding for another drug marker, for example, neomycin resistance and selected in the presence of the drug G418. Screening for intact antibody is accomplished by ELISA assay. 96-well plates are coated with, for example, goat anti-human Fc and detected with, for example, goat anti-human light chain conjugated to alkaline phosphatase.

EXAMPLE 1 AND COMPARATIVE EXAMPLES

[0055] The superiority of the presently claimed method for determining how to modify a rodent antibody or fragment thereof by resurfacing in order to produce a humanized rodent antibody will now be described by reference to the following example and comparative examples which are illustrative and are not meant to limit the present invention.

A) Analysis for Murine Antibodies

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[0056] In order to determine the positions which are usually accessible on the surface of the F_v domain of murine antibodies, the accessibility was calculated for twelve Fab x-ray crystallographic structures obtained from the Brookhaven database (Bernstein, F., Koetzle, T., Williams, G., Meyer, E., Brice, M., Rodgers, J., Kennard, O., Shimanouchi, T. and Tasumi, M. (1977), J. Mol. Biol. 112, pp. 535-542). The relative accessibility was calculated using the program MC (Pedersen, J. (1991)), which implements a modified version of the DSSP (Kabsch, W. and Sander, C. (1983), Biopolymers 22, pp. 2257-2637) accessibility calculation routine in which explicit atomic radii are specified for every atom. A residue was defined as being surface accessible when the relative accessibility was greater than 30%. The alignment positions of these residues were conserved in all twelve structures (98% identity). Surface accessions

sible framework positions constitute 40% of the F_v surface area. The remaining surface accessible residues are in the CDRs and in the interdomain C-terminal region. Figures 3A and 3B show a sequence alignment of the twelve crystal structures, the average relative accessibility, and the 30% accessibility cutoff. Figure 3A shows the alignments relative accessibility for the twelve antibody light chains and Figure 3B shows the alignments and relative accessibility for the antibody heavy chains.

[0057] The surface accessible framework positions were mapped onto a database of unique human and mouse F_{ν} sequences (see lists at the end of this Example). The frequency of particular residues in each of these positions is shown in Table 1. Only residue frequencies higher than 5% are listed.

Table 1:

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Distribution of accessible residues in murine and human V_H and V_L chain sequences. All of the positions appear to be conserved which leads to the hyphothesis that immunogenecity arises from a specific combination of these surface residues. The sequence numbering is explained in Figures 3A and 3B.

	341400 10014403. 11	Light chain	
15			
	Position	Human	Mouse
	1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6
	3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5
20	5	T 61 L 37	Т 87
	9	P 26 S 26 G 17 A 14 L 7	S 36 A 29 L 17 P 5
	15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
	18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9
	46	P 94	P 82 S 9
25	47	G 89	G 71 D 18
	51	K 43 R 31	K 70 Q 13 R 8 T 5
	63 .	G 91	G 98
	66	D 43 S 25 A 9	D 38 A 26 S 26
30	73	S 96	S 90 I 5
	76	D 43 T 18 S 16 E 15	D 67 S 15 A 5 K 5
	86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6
	87	E 71 D 11 G 7	E 91 D 6
	111	K 74 R 12 N 6	K 93
35	115	′ K 54 L 40	K 87 L 5
	116	R 60 G 33 S 5	R 89 G 9
	117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5
	*	Heavy chain	
40	Position	Human	Mouse
	118	E 47 Q 46	E 59 Q 29 D 10
	120	Q 83 T 7	Q 68 K 26
	122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
45	126	G 54 A 23 P 18	G 36 P 30 A 29
	127	G 53 E 22 A 14 D 7	E 45 G 43 S 6
	128	L 61 V 31 F 7	L 96
	. 130	K 46 Q 41 E 5	K 52 Q 27 R 17
50	131	P 95	P 91 A 5
50	132	G 74 S 16 T 7	G 82 S 17
	136	R 53 K 23 S 17 T 7	K 66 S 17 R 13
	143	G 96	G 98
	. 145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5
55	160	P 84 S 10 _.	P 89 H 7
!	161	G 93	G 71 E 24
	162	K 76 Q 10 R 8	. K 50 Q 30 N 10 H 5

Table 1: (continued)

Distribution of accessible residues in murine and human V_H and V_L chain sequences. All of the positions appear to be conserved which leads to the hyphothesis that immunogenecity arises from a specific combination of these surface residues. The sequence numbering is explained in Figures 3A and 3B.

	Heavy chain	
Position	Human	Mouse
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6
196	S 91 ⁻	S 76 A 16
. 197	K 65 I 8 T 8 R 5	S 46 K 34 Q 11
208	R 46 T 18 K 17 D 6	T 55 R 26 K 8
209	A 50 P 21 S 13 T 8	S 67 A 14 T 11
, 210	E 46 A 18 D 13 S 9 Z 8 V 5	E 88 D 7
212	T 91	· T 53 S 43
222	G 17 D 11 P 10 Y 9 V N 8	D 67 A 18

[0058] None of the entire combinations of surface residues in the human sequences are found in the murine sequences and *vice versa* (see lists at the end of this Example). However, the residues in individual positions appear to be conserved (see Table 1). There are few residues which differ significantly between the species; these are at positions 54 and 91 of the L chain and 168 and 216 of the H chain. Of these positions only position 216 is a non conservative (V to Y) mutation. Differences between human and murine antigenicities are therefore believed to arise from the combinations of residues in these positions.

[0059] In order to determine whether the mouse sequences are more distantly related to human F_v sequences than to other mouse F_v sequences, the homology was calculated using a Dayhoff mutation matrix (Dayhoff, M., Barker, W. and Hunt, L. (1983), Meth. Enz. 91, pp. 524-545). The homology was calculated between all the sequences in a pool of both human and mouse sequence patches made up of the surface accessible residues. The data was then represented as a density map (not shown) in which the sequences are plotted against each other. The density map can be used to discriminate "murine surfaces" from "human surfaces".

B) Reshaping of Antibody N901

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[0060] In order to test the resurfacing approach suggested by the above analysis, three humanization experiments were set up. 1) Traditional loop grafting (Verhoeyen, M.E., Saunders, J.A., Broderick, E.L., Eida, S.J. and Badley, R. A. (1991), Disease markers 9, pp. 3-4) onto a human F_v framework of known structure (KOL). 2) Resurfacing approach using most similar chain. 3) Resurfacing approach using human sequences with most similar surface residues.

[0061] The antibody used was the murine anti-N901 antibody (Griffin et al. (1983), J. Imm. 130, pp. 2947-2951). The anti-N901 antibody (also referred to herein as the "N901 antibody") is available commercially from Coulter Corporation under the name NKH-1.

[0062] The alignment of the light chain sequences and heavy chain sequences in Figures 4A and 4B, respectively, show the original N901 antibody and the sequences used in each of the three approaches outlined here.

[0063] Figures 4A and 4B show alignments of sequences generated using the three methods of humanization. Sequences are: 1) Original rodent N901. 2+3) KOL (Marquart, M. Deisenhofer, J. and Huber, R. (1980), J. Mol. Biol. 141, pp. 369-391) and reshaped N901 using KOL surface. 4+5) Most homologous sequences, L(KV2F) (Klobeck, H., Meindl, A., Combriato, G., Solomon, A. and Zachau, H. (1985), Nucleic Acids Res., pp. 6499-6513) and H(G36005) (Schroeder, H. and Wang, J. (1990), Proc. Natl. Acad. Sci. U.S.A. 87) and reshaped N901 using these sequences. 6+7) Most homologous with respect to surface residues, L(KV4B) (Klobeck, H., Bronkamp, G., Combriato, G., Mocikat, R., Pohelnz, H. and Zachau, H. (1985), Nucleic Acids Res. 3, pp. 6515-6529) and H(PLO123) (Bird, J., Galili, N., Link, M., Sites, D. and Sklar, J. (1988), J. Exp. Med. 168, pp. 229-245), and reshaped N901 using these sequences. The numbering is the same as used in the antibody modelling program ABM (ABM is a trademark for commercial software.

bering is the same as used in the antibody modelling program ABM (ABM is a trademark for commercial software, Oxford Molecular Ltd., Oxford, U.K.), which is based on structural conservation and not sequence homology as used by Padlan et al. (Kabat, E.A., Wu, T.T., Reid-Miller, M., Perry, H.M. and Gottesman, K.S. (1987), Sequences of Proteins

of Immunological Interest. U.S. Department of Health and Human Services, Fourth Edition). The sequence changes which have to be introduced in order to reshape N901 with a given sequence are marked with bars, and back-mutations as determined from F_v models are marked with stars. The sequence homology of a given sequence to N901 is shown in brackets after each sequence.

(1) Classical Humanization

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[0064] In classical humanization the rationale is to graft the rodent CDR's onto a framework of known structure, such that CDR-framework interactions can be accurately monitored by homology modelling. The model of the humanized antibody is compared to that of the original rodent antibody, and possible CDR interacting framework residues are back mutated (marked with '*' in alignment) in order to retain the three-dimensional shape of the CDR's. In this example the antibody KOL was used, giving a low homology score of only 77 and 46 in the heavy and light chains respectively.

(2) Most Similar Chain Resurfacing

[0065] A database of nonredundant human antibody sequences was compiled from available protein and nucleotide sequences. A total of 164 H and 129 L chains were sampled.

[0066] Each of the rodent chains, L and H, were then matched and the most similar human sequence found independently (G36005/KV2F) (Schroeder, H. and Wang, J. (1990), Proc. Natl. Acad. Sci. U.S.A. 87); Klobeck, H., Meindl, A., Combriato, G., Solomon, A. and Zachau, H. (1985), Nucleic Acids Res., pp. 6499-6513). Surface residues, as outlined in Table 1, were then changed in the rodent sequences to match those of the human sequences. Subsequently a model was built of the resurfaced antibody and compared to the model of the original rodent antibody and back mutation of any CDR interacting residues was performed.

(3) Most Similar Surface Replacement According to the Present Invention

[0067] This method is identical to the above method, except that the similarity is calculated only over the surface residues outlined in Table 1 above.

[0068] The same procedure of surface mutation and subsequent back mutation was performed as in the previous methods. In this case the chosen sequences were PLO123/KV4B (Bird, J., Galili, N., Link, M., Sites, D. and Sklar, J. (1988), J. Exp. Med. 168, pp. 229-245); Klobeck, H., Bronkamp, G., Combriato, G., Mocikat, R., Pohelnz, H. and Zachau, H. (1985), Nucleic Acids Res. 3, pp. 6515-6529).

[0069] The following lists show the surface residue patterns in mouse and human light and heavy chain antibody variable regions. The sequences are ordered on similarity to one another. There are no pattern matches between mouse and human sequences although there are matches within a species.

HOUSE LIGHT CHAIN SURFACE PATCHES

	1	KVSESMOUSE	:KTSLRPGKGSSDYEKK*	(SEQ	ID	NO:	401
5	2	PL0101		(SEQ	ID	NO:	411
		N\$1F19L		(SEQ	ID	NO:	421
	4	KV5U\$MOUSE	:QTSLRPDKGSSDQEKK*	(SEQ			
•	5	MUSIGLDD		(SEQ			
	6	PL0220		(SEQ			
10	7	KV5J\$MOUSE		(SEQ			
		MUSIGKABB		(SEQ			
•	9	MUSIGKCLG	:QTSLRADKGSSDQEXX*	(SEQ			
		MUSIGGVJ2		(SEQ			
		Musigkern		(SEQ			
. 15		Musickclf	:OTSLKPGRGSSDPEKK*	(SEQ			
•		Musickach		(SEQ			
	14	Musigkabe	:QISLRPGKGSSDSEXX*	(SEQ			
	15	KV5P\$MOUSE	: QTSLRPGKGDSDEDKK*	(SEQ	ID	NO:	54)
	16	MUSIGKCMK	: ETALRPGKGASDADKK*	(SEQ	ID	NO:	55)
20		KV3D\$MOUSE	: VTALRPGKGASDEDKK*	(SEQ	ID	NO:	56)
		Musigkaaw	: VTALRPGKGASDEEKK+	(SEQ			
		KVJGSHOUSZ	:VTALRPGKGASBABKK+	(SEQ			
		KV3 E SMOUSE	: \talrpgkgasdedde•	(SEQ			
	_ 21	Musickaaz	: (ITSLRPDKGSSDQETT*	(SEQ			
25		Musigrone	: Qnsltpgkgsssp zick •	(SEQ			
	23	Musigkba Kvsasmouse		(SEQ			62)
			: VTKVRPGKGDSDAEKK*	(SEQ	ID	NO:	63)
		HUSIGKV	: VTRVRPGKGDSDAEKK*	(SEQ	ID	NO:	64)
		MUSIGRONM		(SEQ			
30		MUSIGKCL1		(SEQ			
30		KV5B\$HOUSE		(SEQ			
		MUSIGROSA -		(SEQ			
	30	Musigkes r Musigkes t		(SEQ			
	32	MUSIGKAB		(SEQ			
35		PL0014		(SEQ			
33		MUSIGRACU		(SEQ			•
		PS0023		(SEQ			73)
		NS 2MCPL		(SEQ			
		MUSIGRADY		SEQ			
40		MUSIGROPP		SEQ			77)
40		MUSIGLDB		(SEQ			•
		MUSIGECHS		SEQ			
		B27887		SEQ			
		H28840		SEQ			
		KV2G\$HOUSE		SEQ			
45		C27887		SEQ			
		JL0029		SEQ			
		MUSICKAER		SEQ			
•		PS0074		SEQ			
		MUSICKCNY		SEQ			
50		MUSIGRONX		SEQ			
		KV2D\$MOUSE		SEQ			
		•		_			-

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:ESSARPGKGDSDAEKK* (SEQ ID NO: 90)
:VTLSSPGQGDSDAEKK* (SEQ ID NO: 91)
:VTTAKPEKGDSDVEKK* (SEQ ID NO: 92)
:VTTPKPDKGDSDVEKK* (SEQ ID NO: 93)
:VTAPRPGKGASSAEKK* (SEQ ID NO: 94)
                 51 MUSIGRADW
                 52 KV2ASHOUSE
                 53 KV1ASMOUSE
                 54 F30534
                 55 MUSIGKCLO
                                                                       :VTAPKPGKGTSSAEKK* (SEQ ID NO: 95)
:VTTPKPGKGASSAEKK* (SEQ ID NO: 96)
:VSAPKPGKGASSAEKK* (SEQ ID NO: 97)
                 56 G27887
                 57 MUSIGVKV3
                 58 MUSIGKCNA
                                                                                                                                         (SEQ ID NO: 97)
                                                                   : VTAPRSGKGASSAEKK*
: VTAPKSGKGASSAEKK*
: VTAPKPDKGVSSAEKK*
: VTAPKSEKGVSSAEKK*
: FTAPKPGKGASSAEKK*
: LTAPKPGRGVSSAEKK*
10
                 59 S03410
                                                                                                                                         (SEQ ID NO: 98)
                 60 B32456
                                                                                                                                       (SEQ ID NO: 99)
                 61 PL0013
                                                                                                                                          (SEQ ID NO: 100)
                62 MUSIGLAET
                                                                                                                                          (SEQ ID NO: 101)
                 63 MUSIGVKV1
                                                                                                                                           (SEQ ID NO: 102)
                64 KV6K$MOUSE.
                                                                 :LTAPKPGRGVSSAEKK* (SEQ ID NO: 103)
:VTAPKSGKGASSAEKK* (SEQ ID NO: 104)
:VSAPKPGKEGSSAEKK* (SEQ ID NO: 105)
:VTAPKPRKGASSAEKK* (SEQ ID NO: 106)
:VTFLSPGQGNSDAELP* (SEQ ID NO: 107)
:VTFLSPGQGNSDEDLP* (SEQ ID NO: 108)
:VTLSSPGRGDSDAEKK* (SEQ ID NO: 109)
:VTAPKSSKGGSSAEKK* (SEQ ID NO: 110)
:QTSPTPGKGSSDPEKK* (SEQ ID NO: 111)
:QISLIPGKGSYDDEKK* (SEQ ID NO: 112)
:VTALKSGKGASSAEKK* (SEQ ID NO: 113)
                                                                                                                                           (SEQ ID NO: 103)
                65 G30560
                66 MUSIGKBO
                67 MUSIGKCNB
                68 H33730
               69 MUSIGKCPC
20
                70 KV2C$MOUSE
             -71 MUSIGLAV
                72 MUSIGKONH
               73 KV5R$MOUSZ
                                                                  :QISLIPGKGSYDDERR*
:VTALKSGKGASSAEKK*
:VTALKSDKGASSGEKK*
:VTALKSDKGASSGEKK*
:VTPPSPGQGDSAAEKK*
:VTPPSPGQGDSAAEKK*
:VTPPSPGQGDSAEKK*
:VTVRKPGKGDSSDEKK*
:VTVRKPGKGDSSDEKK*
:VTVRKPGKGDSSDEKK*
:QTSVRLGQGSSDPEKK*
:QTSVRLGQGSSDPEKK*
:QTDVTGGQGSSQPEKK*
:QTDVTGGGSSQPEKK*
:QTDVTGGQGSSQSEKK*
:QEQ ID NO: 119)
:QTAVSQGGGSSQSEKK*
:SEQ ID NO: 120)
:LTAPRTNRGSSDSEKK*
:SEQ ID NO: 121)
:LTAPRTNRGSSDSEKK*
:SEQ ID NO: 123)
:LLSLSPLKGDSDPEKV*
:VTAPTPDTGAIKTEKL*
:VTAPTPDTGAIKTEKL*
:AVSPTPDTGAIKTEKL*
:AVSPTPDTGAIKTEKL*
:AVSPTPDTGAIKTEKL*
:AVSPTPDTGAIKTEKL*
:SEQ ID NO: 128)
:AVSPTPDTGAIKTEKL*
:SEQ ID NO: 129)
:AVSPTPDTGAIKTEKL*
:SEQ ID NO: 129)
:AVSPTPDTGAIKTEKL*
:SEQ ID NO: 129)
               74 KV6ESHOUSE
                75 MUSIGRONI
               76 MUSIGLDA
77 C26317
78 PS0073
79 A23986
30
                79 A23986
               80 MUSIGRABW
81 KV5D$MOUSE
               82 MUSIGEGL
83 MUSIGECOE
35
               84 HUSIGKCKN
85 HUSIGLVD
86 S06822
87 S06821
88 HUSIGLAS
               89 MUSICIAR .
               90 LYZB$NOUSE
               91 MUSIGLAN
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HUMAN LIGHT CHAIN SURFACE PATCHES.

```
1 LV4ASHUMAN
                                                                                                               :ILPPTPGVIRSTAMKL* (SEQ ID NO: 131)
:YLPPTPGVIRSTAMRL* (SEQ ID NO: 132)
:YLPPTPGLIRSTSMKL* (SEQ ID NO: 133)
:YLPPTPGLIRSTSVKL* (SEQ ID NO: 134)
:YLPPTPGVIRSTAEKL* (SEQ ID NO: 135)
:YLPPTPGVIRSTAGKL* (SEQ ID NO: 136)
:YLPATPGVVRSSAGML* (SEQ ID NO: 137)
                                                                                                                  :YLPPTPGVIRSTAMKL*
                                                                                                                                                                                                 (SEQ ID NO: 131)
                              2 LV4BSHUMAN
5
                              3 LV4ESHUMAN
                                                                                                               :YLPPTPGLIRSTSMKL*
                                                                                                              :YLPPTPGLIRSTSVKL*
                              4 LV4DSHUMAN
                                                                                                         :YLPPTPGVIRSTAEKL*
:YLPPTPGVIRSTAGKL*
:YLPATPGVVRSSAGHL*
:SLPATPGVVRSSAGHL*
:SLPPSPGKVRSTAEKL*
:SLPPSPGKVRSTAEKL*
:SLPPSPGKVRSTAEKL*
:SLPPSPGKVRSSSEKL*
:SLPPRPGKVRSSSEKL*
:SLPPRPGKVRSSSETL*
:SLPPRPGKVRSSSETL*
:SLPPRPGKIRSSTGKL*
:SLPPRPGKIRSSTGKL*
:SLPPRPGKIRSSTGKL*
:SLPPRPGKIRSSTGKL*
:SLPPRPGKIRSSTGKL*
:SLPPRPGKIRSSTGKL*
:SLPPRPGKIRSSTGKL*
:SLPPRPGKIRSSTGKL*
:SLPPRPGKIRSSTGKL*
:SLPPRPGKIRSSTGNV*
:SLPPRPGKIRSSTGNV*
:SLRPSPGKVRSTAEKL*
:SLRPSPGKVRST
                                                                                                              :YLPPTPGVIRSTAEKL*
                              5 LV4CSHUMAN
                                                                                                              :YLPPTPGVIRSTAGKL*
:YLPATPGVVRSSAGHL*
:SLPPSPGKVRSTAEKL*
:SLPPSPGKVRSTANKL*
                              6 LV5A$HUMAN
                              7 LV7ASHUMAN
10
                         8 LV2G$HUMAN
                            9 LV2ISHUMAN
                          10 NS2RHE
                        11 HUMIGLAN
                                                                                                     :Slpprpgkvrsssdkl*
:Slpprpgrvrsssekl*
:Slpprpgkvrssseql*
:Slpprpgkvrsssettl*
:Slpprpgkirsstgkl*
:Slpprpgkirsstgkl*
:Slpprpgkirsstgkl*
:Slpprpgkirsstgkl*
:Slpprpgkirsstgkl*
:Slpprpgkirsstgkl*
:Slpprpgkirsstgkl*
                         12 LV1ASHUMAN
                         13 LV1BSHUMAN
                         14 LV1PSHUMAN
                         15 LV1CSHUMAN
                         16 A29700
                         17 HUNIGLANA
                        18 LV1D$HUMAN
20
                                                                                                        : Slapspgkirstaekl*
: Slapspgkirsstghv*
: Slrpspgkvrstaekl*
: Slrpspgkvrstadkl*
                         19 LV2KSHUMAN
20 LV1ISHUMAN
                          21 LV2ESHUMAN
                          22 LV2DSHUHAN
                          23 LV2C$HUNAN
                         24 LV2JSHUMAN
                        25 LV1ESHUMAN
                         .26 LV2B$HUKAN
                       27 NSINCW
                       .28 LV2HSHUMAN
30
                        .29 N$3MCG2 -
                       30 LV2ASHUMAM
                         31 902083
                         32 HUNIGLAN2
                                                                                                                                                                                         (SEQ ID NO: 162)
(SEQ ID NO: 163)
(SEQ ID NO: 164)
(SEQ ID NO: 165)
(SEQ ID NO: 166)
(SEQ ID NO: 167)
(SEQ ID NO: 168)
(SEQ ID NO: 169)
(SEQ ID NO: 170)
                         33 LV6CSHUMAN
                                                                                                              : FLLPTPGTDSSSTERL*
                         34 LV6DSHUMAE
                                                                                                            : Plhptrvtdssstekl*
: Llpptpgthsssndkl*
: Vlplsphrirsesenl*
                         35 LV6ESHUMAN
                         36 LV68$HUMAN
37 HUMIGLK5G
                                                                                                            : SLAPSPAKTRSTAERD*
                         38 HUNIGLYC.
                                                                                                            :VTAPRPGRIRSDPEKK*
                         39 HUMIGVLLS
                     40 HUNCIGKAX
                                                                                                           :VTAPRPGRVRSDPEKK*
                                                                                                  :VTGPRPGRIRSDPEK*
:VTGPRPGRIRSDPDKK*
:VTGPRPGRIRSDPDKK*
:VTGPRPGRIRSDPEKK*
:VTGPRPGRIRSDPEKK*
:VTAPRPGRIRSDPEKK*
:VTAPRPGRIRSDPEKK*
:VTYPRPSRIRSBSERK*
:VTVPRPSRIRSBSERK*
:VTVPRPSRIRSBSERK*
:VTAPGPGRIRSBSERK*
:QTSVRPGRVRSDPEKK*
:QTSVRPGKVRSDPEKK*
(SEQ ID NO: 177)
:QTSVRPGKVRSDPEKK*
(SEQ ID NO: 178)
:QTSVRPGKVRSDPEKK*
(SEQ ID NO: 179)
:QTSVRPGKVRSDPEKK*
(SEQ ID NO: 180)
                         41 E30609
                                                                                                            :VTGPRPGRIRSDPEKK*
                                                                                                                                                                                                   (SEQ ID NO: 171)
                         42 KV3BSHUKAN
                         43 G30607
                         44 KV3MSHUMAM
45
                         45 KV3HSHUMAN
                         46 KV3KSHUMAN
                   47 KV3F$HUNAN
                       48 B26555
                       49 KV1Q$HUMAN
                  50 KV1WSHUMAN
```

```
51 KVIMSHUMAN
                                  :QTSVRPGKVRSDPEKK*
                                                          (SEQ ID NO: 181)
                                  :QTSVRPGKVRSEPEKK*
                                                          (SEQ ID NO: 182)
        52 KVLRSHUMAN
                                  :QTSVRPGKVRSEPDKK*
                                                          (SEQ ID NO: 183)
        53 KV1FSHUMAN
                                  :QTSVRPGKVRAEPEKK*
                                                          (SEQ ID NO: 184)
        54 KV1G$HUHAN
        55 KV1K$HUMAN
                                  :QTSVRPGKVRSBPZKK*
                                                          (SEQ ID NO: 185)
        56 KV1D$HUMAN
                                  :QTSVRPGKVRSDPBKK*
                                                          (SEQ ID NO: 186)
                                                          (SEQ ID NO: 187)
        57 KV1H$HUMAN
                                  :QTSVRPGQVRSDPERK*
        58 KV1B$HUMAN
                                  :QTSVRPGKVRSHPEXK*
                                                          (SEQ ID NO: 188)
10
        59 B27585
                                  : OTSVRPGNVRSDPDKK*
                                                          (SEQ ID NO: 189)
                                                          (SEQ ID NO: 190)
        60 NSIREIA
                                  :QTSVRPGKVRSDPEKT*
                                  :QTSVRPGTVRSEPEKK*
                                                          (SEQ ID NO: 191)
        61 KV1XSHUMAN
                                  :QTSVRPEKVRSEPDKK*
                                                          (SEQ ID NO: 192)
        62 KVILSHUMAN
                                  : QTSVRPGKVRSESDKK*
                                                          (SEQ ID NO: 193)
        63 IMGL38
15
                                  :QTSVRPGEVRSEPDKK*
                                                          (SEQ ID NO: 194)
        64 A27585
                                  :OTSVRPGBVRSBPZRK*
        65 KVINSHUMAN
                                                          (SEQ ID NO: 195)
                                  :QTSVSPGKVRSDPEKK+
        66 KV1CSHUMAN
                                                          (SEQ ID NO: 196)
                                  :QTSVRPGKVNSDPEKK*
        67 KV1VSHUMAN
                                                          (SEQ ID NO: 197)
                                  :OTSVRPGKVRSDPDTK*
                                                          (SEQ ID NO: 198)
        68 KVITSHUMAN
                                  :QTSVRPKKVRSDPZKK*
        69 KV1USHUMAN
                                                          (SEQ ID NO: 199)
20
                                  :QTSVRPKKVRFDPEKK*
                                                          (SEQ ID NO: 200)
        70 KVIASHUMAN
                                  :QTSVRSGKVRSEPETK*
                                                          (SEQ ID NO: 201)
        71 KV1SSHUMAN
                                  :VTNLRPGKVRSDAEKK*
                                                          (SEQ ID NO: 202)
        72
           KV4ASHUMAN
                                  :VTDLRPGKVRSDAEKK*
                                                          (SEQ ID NO: 203)
        73 KV4C$HUMAN
                                  :OTSVSPGNIRSESDKK*
                                                          (SEQ ID NO: 204)
        74 HUNIGK2AL
25
                                  :KTSVTPGKFRSEPEKK*
                                                          (SEQ ID NO: 205)
        75 HUNIGKBA
                                  :VTLLPPGRVRSDAEKK*
                                                          (SEQ ID NO: 206)
        76 HUNIGKBC
                                  :VTLLPPGEVRSDAZKK+
                                                          (SEQ ID NO: 207)
        77 KV2BSHUMAN
                                  :VTLPPPGZVRSDAERK+
                                                          (SEQ ID NO: 208)
        78 KV2DSHUMAN
                                                          (SEQ ID NO: 209)
                                  :VTLPPPGZVRSBAZNK*
        79 KV2C$HUKAN
                                  :VTLPPPQQVRSDAERK*
                                                          (SEQ ID NO: 210)
30
        80 KVZESHUKAN
                                  :VTLPPPGQVTSDAEKK+
                                                          (SEQ ID NO: 211)
        81 S03876 ....
                                  :VTEPPAGQVRSDAERR+
                                                          (SEQ ID'NO: 212)
        82 KV2ASHUMAE
                                  :ALSPSSGQSSSASERL*
                                                          (SEQ ID NO: 213)
        83 HUMIGLAMS
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HOUSE HEAVY CHAIN SURFACE PATCHES

```
(SEQ ID NO: 214)
                  1 MUSIGHIT
                                                                 : EKVGGLQPGRGTPGKASRGDSQRPES*
                                                                                                                                  (SEQ ID NO: 215)
                                                                 : EKVGGLQPGRGTPGKVSRGDSQRPES*
                   2 MUSIGHIU
5
                                                                : EKVGGLQPGTGAPGKASRGDSQRPES •
                                                                                                                                  (SEQ ID NO: 216)
                  3 MUSIGHIV
                                                                                                                                  (SEQ ID NO: 217)
(SEQ ID NO: 218)
                   4 MUSIGHYM
                                                                : EKVGGLQPGRGTPGKASKGNSQRAES*
                                                                : EKMGGLQPGRGTPGKASKGNSQRAES*
                  5 PU0003
                                                              : EKYGGLQPGRGTPGKASKGTSQRAES*
                                                                                                                                  (SEQ ID NO: 219)
                   6 MUSIGHFO
                                                             : EKVGGLQPGRGTPGKASKGTSQRAET*
                                                                                                                                  (SEQ ID NO: 220)
                  7 A30515
                                                           : EKVGGLKPGRGTPGKASKGTSGRAET+
: ENVGGLQPGRGTPGKASKGTSQRAET+
                                                                                                                                  (SEQ ID NO: 221)
(SEQ ID NO: 222)
                  8 PL0018
10
                9 MUSIGHFK
                                                                                                                                 (SEQ ID NO: 223)
                                                                : EXVGGLQSGRGTPGKASKGTSQRAET®
                10 MUSICHPQ
                                                            : EXVGGLOSGRGTPGKASKGTSQRAES*
                                                                                                                                  (SEQ ID NO: 224)
(SEQ ID NO: 225)
                11 PU0001
                                                              : EKVGGLQPGRGTPGKASKGISQRAER*
: EKVGGLQPGRGTPGKSAKGBSZRAQS*
: EKVGGLQPGSGTPGKASKGNSQRAES*
                12 E30540
                                                                                                                                  (SEQ ID NO: 226)
                13 HV17SHOUSE
                14 MUSIGHLN
                                                                                                                                  (SEQ ID NO: 227)
15
                                                              : ekvgglopgsgtpgkaskgssgraes*
: ekvgglopgrgtprkaskgnsgraes*
                                                                                                                                  (SEQ ID NO: 228)
(SEQ ID NO: 229)
                15 MUSIGHKG
                16 PUOOO4
17 MUSIGHRJ
                                                              : EXCEPTION OF THE PROPERTY OF
                                                                                                                                  (SEQ ID NO: 230)
                                                                                                                                  (SEQ ID NO: 231)
                                                                : EKVGGLAPGKGTPEKDSKGNARRSET+
                18 HV56SMOUSE
                                                                                                                                  (SEQ ID NO: 232)
(SEQ ID NO: 233)
                                                                 : EXVGGL&PGKGAPEKDSKGNARRSET*
                19 C27888
                                                                : EXVGGLKPGKGTPERDSKGNARRSET+
                20 MUSIGHAAP
20
                                                               : DKVGGLKPGKGTPEKDSKGNAKRSET+
                                                                                                                                  (SEQ ID NO: 234)
                21 PH0097
                                                              : DKVGGLKPGKGTPEKDSKGNAKKSET+
                                                                                                                                  (SEQ ID NO: 235)
(SEQ ID NO: 236)
                22 E27888
                                                             : DKVGGLKPGKGTPDKDKKGHAKKSET•
                23 MUSICHJB
                                                                                                                                  (SEQ ID NO: 237)
(SEQ ID NO: 238)
(SEQ ID NO: 239)
                                                                 : EKVGGLTPGKGTPEKDSKGNGRRSET*
                24 MUSIGHADL
                                                           : Envegledgretdergndrebet*
: Envegledgretdergndrebet*
: Envegledgretdergndrebet*
                25 A27888
                26 H27887
25
                                                                                                                                  (SEQ ID NO: 240)
                27 827888
                                                              : BOVGGLEPGKGTPEKDSKGNAKKSET+
                                                                                                                                  (SEQ ID NO: 241)
                28 B27889 ·
                                                                 : EQVGGLKPGKGTPEKDTKGHAKKSET+
                                                                                                                                  (SEQ ID NO: 242)
                29 D27889
                                                                 : BOVGGLEPGRGAPERDTRGHARKSET+
                                                                                                                                  (SEQ ID NO: 243)
                30 HV55SMOUSE
                                                                                                                                  (SEQ ID NO: 244)
(SEQ ID NO: 245)
(SEQ ID NO: 246)
                                                                 : EKYGGLOPGKGTPEKDSKGNAKKSET+
                31 MUSIGHAGT
                                                                 : EXVGGLOPGKGTPEXDTRGKAKKSET*
                32 MUSIGVHSO
30
                                                                 : EKVGGLQPGRGTPERDTKGNAKKSET+
                33 MUSIGHIW
                                                                 : EKVGGLOPGKGSPEKDSKGKAKKSET*
                                                                                                                                  (SEQ ID NO: 247)
                34 MUSICHAGE
                                                                                                                                  (SEQ ID NO: 248)
(SEQ ID NO: 249)
                                                                 : DIOIGGLEPGEGTPEEDSEGHARQSET*
                35 PH0098
                                                                  : DOVGGLOPGRGTPDKDSKGNAKKSET+
                36 MUSICHID
                                                                                                                                  (SEQ ID NO: 250)
                                                                 : EKVCGLOPGRGTPEXDSKGHARKSET*
                17 MUSIGHAGE
                                                                 : EQVGDLKPGKGTPEKDTKGNARRSET+
                                                                                                                                  (SEQ ID NO: 251)
                38 MUSIGHOET
35
                                                                                                                                  (SEQ ID NO: 252)
(SEQ ID NO: 253)
                                                                  : ZHVGDLKPGKGAPEKDSKGHARRSET*
                39 D27888 -
                                                                  : EQVGGLOPGKGTSDKDSKGHAKKSET*
                40 MUSIGHIP
                                                               : EQVGGLQPGKGTPEKDSKGNAKKSGT*
                                                                                                                                   (SEQ ID NO: 254)
                41 HUSIGHAGS
                                                                 : DQVGGLQPGRGTPEKDTKGHPKRSET*
                                                                                                                                   (SEQ ID NO: 255)
                42 HV16$MOUSE
                                                                                                                                   (SEQ ID NO: 256)
                                                                  : DQVGGLQPGQGTPEXHTKGHPKRSDT*
                43 B34871
                                                                                                                                   (SEQ ID NO: 257)
                                                                 : EXVGGLOPGEGTSENDINGNANASET+
                 44 PH0094
                                                                  :DEVGGLEPGERTPERDHEGHARESET+
                                                                                                                                   (SEQ ID NO: 258)
                45 PH0096
                                                                                                                                  (SEQ ID NO: 259)
(SEQ ID NO: 260)
                                                                : DKYGGLKLGKGTPEKDTKGHAKKSET*
                46 MUSIGVH62
                                                               : EKVGGLQPGKGTPEKDSKGNANTSET*
                47 MUSIGHAGE
                                                               : EHVGGLEPGKGTPEKDSKGHAGRSET
                                                                                                                                  (SEQ ID NO: 261)
               48 HV58SMCUSE
                                                                : EQVGGLQPGHGTPEKD/TGHAKRSET*
                                                                                                                                  (SEQ ID NO: 262)
                49 H27888
                                                                                                                                  (SEQ ID NO: 263)
                                                               : EXEGGLOPGROTPEXESKGDSXRAFT*
                50 HV34$MOUSE
45
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51 HV33$HOUSE
                                   : EKEGGLOPGKGTPEKESKGDSKRPET+
                                                                       (SEQ ID NO: 264)
                                                                    (SEQ ID NO: 265)
        52 MUSICHZAB
                                : EKEGGLQPGKGSPEKESKGDSKRAET+
                                                                      (SEQ ID NO: 266)
(SEQ ID NO: 267)
        53 N$4FABH
                                   : EKDGGLQPGKGTPEKDSKGDSKRVEN+
                                   : EQVGGLKPGRGTPEKDTTGDAQRSET+
        54 127888
       ·55 G27888
                                   : EQVGGLKPGRGTPEKDTTGNAKGSET+
                                                                       (SEQ ID NO: 268)
        56 HV59$MOUSE
                                  : EXVGGSKPGKGTPEKDSKGNAKTSET*
                                                                       (SEQ ID NO: 269)
                                 :SDQGGLKPGKGTPEKDTKGNARRSES+
        57 MUSIGHOE
                                                                       (SEQ ID NO: 270)
                                                                       (SEQ ID NO: 271)
(SEQ ID NO: 272)
        58 NS2FVWH
                                  : EKIGGLQPGKGDPGKPSKDNAKRSET+
                                  : eklgglopgkgdpgkpskdnakrset•
        59 MUSICHIT
                                                                       (SEQ ID NO: 273)
        60 MUSICHLY
                                  : EXLGGLQPGKGDPGKPFKDNAKRSET*
 10
                                  : eklgglqpgkgdpgklmkenakrset•
        61 506816
                                                                        (SEQ ID NO: 274)
        62 506817
                                  : ENLGGLOPGKGDPGKLKXENAKRPET+
                                                                       (SEQ ID NO: 275)
        63 MUSIGHAAI
                                  : EKLGGLQPGNGDLGKPSKDNAKRSET*
                                                                        (SEQ ID NO: 276)
                                   : EKLGPLOLGKGDPGKPSKDDAKRSET*
                                                                        (SEQ ID NO: 277)
        64 HV42SHOUSE
         5 MUSIGHAAL
                                   : EQLGGLQPGGGTPGKP9KDNDKR9ET*
                                                                        (SEQ ID NO: 278)
                                                                       (SEQ ID NO: 279)
(SEQ ID NO: 280)
                                   : EQLGGLOPGGGTPGKASKDNDKRSET+
        _6 MUSIGHABO
 15
                                   : EQVGGLKARKGTPEKDTTGNAKRSET*
        67 MUSIGHEG
                                : envgvlepgkgtpekrgegnakreet*

: eqvgglqpkkgspgkdskddsqktet*

: eqvgglqpkkgspgkdskddsqkter*
        68 MUSICHWN
                                                                        (SEQ ID NO: 281)
        69 MUSICKCLT
                                                                       (SEQ ID NO: 282)
(SEQ ID NO: 283)
(SEQ ID NO: 284)
        70 MUSIGHZAE
                                   *QQVPELKPGRGTPGKEDKGT9ARNDT*
        71 HUSIGHAAD
                                   :QQVPELKPGKGTPGKDDKGTSAKNET*
                                                                        (SEQ ID NO: 285)
        72 MUSIGHAAN
 20
        73 MUSIGHAMA
                                   :QQVPELKPGKGTPGKDDKGTSAKNEM*
                                                                        (SEQ ID NO: 286)
                                                                        (SEQ ID NO: 287)
(SEQ ID NO: 288)
        74 MUSIGHXZ
                                   : QQKPELKPGKGSPGQEXKGTSSTSET*
                                   : EQQPELKPGKGTPGQEKKGKSSTSES*
        75 A30502
                                   : EQQPELRPGKGTPGQEKKGKSSTSES*
                                                                        (SEQ ID NO: 289)
        76 MUSIGHAAG
        77 B30502
                                   : POOPELKPGKGTPGQEKKGKSSASES*
                                                                        (SEQ ID NO: 290)
 25
        78 MUSIGHADG
                                   : EQQPELKPGKGTPGKQKKGKSSTSZS*
                                                                        (SEQ ID NO: 291)
                                                                        (SEQ ID NO: 292)
                                   : EQQPELXPGXGTHGXQXXGXSSTSES*
        79 MUSIGHTV
                                   : EQQPELKPGKGSHGKQKKGKSSTSES*
        80 MUSIGHAANA
                                                                        (SEQ ID NO: 293)
                                                                        (SEQ ID NO: 294)
(SEQ ID NO: 295)
        81 MUSIGHER
                                   : ECOPELKPGKGSEGKOKKGKSSASES*
                                   : EQQPELKPGKGTHGKQKKGKSSTFES*
        82 MUSIGHAI
                                                                       (SEQ ID NO: 296)
        83 MUSICHALA
                                   : POOPELKPGKGTHGKQKQGKSSTFES*
        34 PL0011
                                   : EQOPELEPGEGTHGKEKKDESSTSES+
                                                                        (SEQ ID NO: 297)
                                   : BOOARLKPGKGSHGKOKKGKSSTSES+
                                                                        (SEQ ID NO: 298)
        ds MUSICKCLS
                                   : EQQPELKPGKGTHGKQXKSNSSTSES+
        86 MUSIGHADY
                                                                        (SEQ ID NO: 299)
                                   : OCCAPILEPGEGAPGOEICEGESTSES*
                                                                        (SEQ ID NO: 300)
        87 MUSIGENVX
                                   : QQQAELRPGKGAPGQEKKGKSSTSD8+
        88 MUSIGRADO
                                                                        (SEQ ID NO: 301)
                                                                        (SEQ ID NO: 302)
(SEQ ID NO: 303)
                                   :QQQAELRPGKGVPGQEKKGKSSTSDS+
        89 MUSIGHVEM -
. 35
                                   : QQQPELKPGKGAPGKGKKGKSSTSES*
        90 A24672
                                   : QQQPELICPGKGAPGKGKKDKSSTSES*
                                                                        (SEQ ID NO: 304)
        91 MUSICHJO
                                   : EQQPEAKPGKGTHGKQKKGKSSTSDS+
                                                                        (SEQ ID NO: 305)
        92 JL0044
                                                                        (SEQ ID NO: 306)
(SEQ ID NO: 307)
                                   : QQQAELKPGKGTHGKEKKDKSSTSDS*
        93 MUSIGHBA
                                   :QQQAZLRPGKGAPGQGKKGKSSTSES*
        94 MUSIGRAGP
                                   : QQQAELKPGRGTPGQEKKGKSSTSES*
                                                                        (SEQ ID NO: 308)
        95 MUSICHVBK
 40
                                   : EQQAELRAGKGTPGQEKKGKSSTSES*
                                                                        (SEQ ID NO: 309)
        96 A36194
                                                                        (SEQ ID NO: 310)
                                   : POOAELRPGKGTPGQEKKGTSSTSES*
        97 MUSICHVBJ
                                   :QQQAELRPGKGTPGHEKKGTSSTSES*
                                                                        (SEQ ID NO: 311)
        98 MUSICHADV
                                                                        (SEQ ID NO: 312)
                                   : QQQAELEPGKGTPGHEKKGTSSTSES*
        99 MUSICHAAT
                                   :QQQAELRPGKGTPGHENKGTSSTSES*
                                                                        (SEQ ID NO: 313)
       100 MUSICHJL
```

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(SEQ ID NO: 314)
       101 MUSIGHABM
                                     :QQQAEVRPGKGTPGHEXKGTSSTSES+
                                                                            (SEQ ID NO: 315)
                                     : QQQAELKPGKGTPGHENKGTSSTSES*
       102 MUSIGHFU
                                                                            (SEQ ID NO: 316)
                                     : QQQAELRPGKGTPGQQKKGKSSASES*
       103 MUSIGHZZB
                                                                            (SEQ ID NO: 317)
       104 HVO6SHOUSE
                                     : HQQAELKPGKGTPGQQKKGKSSTSES*
                                                                            (SEQ ID NO: 318)
(SEQ ID NO: 319)
                                     : EQQVELRAGKGTPGQEXKGKSSTSES*
       105 MUSIGHRD
       106 MUSIGHVBH
                                     : EQQAELRPGKGTPGQEKQGTSSTSES*
                                                                            (SEQ ID NO: 320)
       107 HV01SHOUSE
                                     : EQQAELRPGKGTPGHDNKGTSSTSES*
                                                                            (SEQ ID NO: 321)
                                     : QQQAEVRPGKGTPGHEXXGRSSTSES*
        108 MUSIGHADN
                                                                            (SEQ ID NO: 322)
(SEQ ID NO: 323)
(SEQ ID NO: 324)
       109 HVOSSMOUSE
                                    : OOGAELRPGKGTPGOOKKDKSSTSES*
10
                                    : QQQAELKPGKGTPGQQKKDKSSTSES*
       110 MUSIGHAEF
                                    : QQQAELKPGKGTPGQQKKDKSSTSDS*
: QQQAELKPGKGSPGQQKKDKSSTSES*
       111 MUSIGHAAN
                                                                            (SEQ ID NO: 325)
        112 MUSIGHAAB
                                                                            (SEQ ID NO: 326)
(SEQ ID NO: 327)
(SEQ ID NO: 328)
(SEQ ID NO: 329)
                                    : QHQAELKPGKGTPGQQKQKKSSTSES*
        113 C30560
                                     : QQQAELKPGKGTPGQQNKDKSSTSES*
       114 PS0024
                                    : Eqqaelragkgipgqexkgksstses*
: qqqaelrpgkgtpgqekksksstses*
: qqqselkpgkgtpgqekksksstses*
15
       115 MUSIGHRG
       116 MUSIGHAAB
                                                                            (SEQ ID NO: 330)
(SEQ ID NO: 331)
       117 MUSIGHLX
                                      : QQQTELXPGKGTPGQEKKSKSSTSES*
       118 HV045MOUSE
                                    : EQQAELRIGKGTPGQERKGKSSTSES•
                                                                            (SEQ ID NO: 332)
(SEQ ID NO: 333)
     . 119 MUSIGHVBG
       120 MUSICHOX
                                      : QQQAELKPGKGTPGQQKKDKSSTPES*
     121 HUSIGHAAR
                                                                            (SEQ ID NO: 334)
20
                                      : EQOAELRPGTGAPGQEKKGKSSTSES*
                                      : QQQPEVRPGKGTHAKQKKGKSSTSES*
                                                                            (SEQ ID NO: 335)
(SEQ ID NO: 336)
       122 HV15$HOUSE
                                      : OOOPEVRPGKDTHAKOKKGKSSTSES*
       123 MUSIGHAAU
                                                                             (SEQ ID NO: 337)
                                      : QQQAELKPGKGTPEQEKKGKSSTSES*
        124 MUSIGHVBO
                                    : EQCTELRAGKGTPGQEXKGRSSTSZA*
                                                                            (SEQ ID NO: 338)
        125 A26405,
                                   : QQQAELKPGKGTPGREKKSKPSTSES*
: QQQSELKPGKGTPGREKKSKPSTSES*
: QQRAELKPGKDTPGREKKKKPSTSES*
                                                                             (SEQ ID NO: 339)
        126 HV10SHOUSE
                                                                             (SEQ ID NO: 340)
25
        127 MUSIG3B44
                                                                             (SEQ ID NO: 341)
        128 MUSIG3B62
                                                                            (SEQ ID NO: 342)
(SEQ ID NO: 343)
(SEQ ID NO: 344)
                                    : QQQAELKPGKGTPGREKKSTSSTSES*
        129 HV09$MOUSE
                                    : QQQAELKPGKGTPGQEKKSTSSTSDS*
        130 MUSIGKCLP
                                      : QQQAELRPGKGTPIQQKXDKSSTSES*
        131 MUSIGBE
                                      :QQQAEFKPGKGTPGREIRSKPSTSES*
                                                                             (SEQ ID NO: 345)
        132 HV11SHOUSE
30
                                    : QQQAELRPGKGALGQEKKGKSSTSDS*
                                                                             (SEQ ID NO: 346)
        133 MUSIGHMC
                                    : QQQPEVKPGKGAPGKGNTDKSSTSES*
                                                                             (SEQ ID NO: 347)
(SEQ ID NO: 348)
        134 MUSIGHAGN
                                    : BOOMEVRAGEGSPGOEKEGESTSES*
        135 MUSIGHRE
                                      :QQLAELXPGKGTPGHEKKGISSTSES*
                                                                             (SEQ ID NO: 349)
        136 MUSICHVAD
                                                                             (SEQ ID NO: 350)
                                      : QQQAELXPGKGKPEQEKKGTSSTSES*
        137 MUSIGHVAF
                                    :QQQPELAPGKGRHGKEKKGKSSTSES*
                                                                             (SEQ ID NO: 351)
(SEQ ID NO: 352)
        138 PL0012
35
                                      :QQQTELRPGRGTTGQERKGKSSTSES*
        139 MUSIGGVD2 ...
                                      : QHQAELKPGKGTPGHENKVTSSTSES*
                                                                             (SEQ ID NO: 353)
        140 506824
                                                                             (SEQ ID NO: 354)
                                     : EQQAELRAGEGTPGQEQEARSSTSES*
      · 141 MUSIGHTS
                                                                             (SEQ ID NO: 355)
                                      : QQQAELEPGKGTPGQQATGTSSTTES.
        142 MUSIGHAAR
                                                                             (SEQ ID NO: 356)
                                      : QQQAELEPGKGNPGQEKKSTSSASES*
        143 MUSIGHES
                                                                             (SEQ ID NO: 357)
                                      : ZQQTVLRPGKGTPGQQKKGTSATNES*
        144 MUSIGHAXA
                                                                             (SEQ ID NO: 358)
(SEQ ID NO: 359)
                                   : QQLTELXPGHGTPGQEXXSXSSTS8S*
        145 HV50$HCUSE
                                    : QQQSVLRPGKGTPGQEKKGTSSTSKS.
        146 MUSICHVBP
                                                                             (SEQ ID NO: 360)
                                      :LQQPVLKPGKGSHGKQKKDKSSTSES+
        147 PHO100
                                      : EQQPETKPGKGTLGKQKKSKSSTSES*
                                                                             (SEQ ID NO: 361)
        148 MUSIGHAYA
                                     : OCCAPILAPGOGTPGOERKHASSTPEF+
: ECCAPILAPGAGHEOPAGGTSSTSET+
                                                                             (SEQ ID NO: 362
        149 MUSIGHCP2 .
                                                                             (SEQ ID NO: 363
```

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150 MUSIGHDZ

```
: EQQAELRPGKGNPEQPKQGTSTTSET+
         151 MUSIGHNPI
                                                                       (SEQ ID NO: 364)
                                    : EQQAELKPGKGNPEQPKQGTSSTSET+
         152 S06823
                                                                       (SEQ ID NO: 365)
                                    : EQQAELKPGKGNPEQPKQDTSSTSET*
         153 MUSICHASA
                                                                       (SEQ ID NO: 366)
                                    : EQQAELKPGKGNPEQPKQGTSSTSGT+
         154 S03484
                                                                       (SEQ ID NO: 367)
 5
                                    : EQQAEVKPGKGNPEQPKQGTSSTSET*
         155 MUSIGHVAA
                                                                       (SEQ ID NO: 368)
                                    : EQQAELRPGKGNPEQPKQVTSSTSET*
         156 MUSIGHNPD
                                                                       (SEQ ID NO: 369)
        157 MUSIGHNPB
                                    : EQQAELRPGKGNPEQPKQITSSTSET+
                                                                       (SEQ ID NO: 370)
                                   : EQQAELRPGRGNPEQPKQVTSSTSET+
         158 MUSIGHEC
                                                                       (SEQ ID NO: 371)
                                    : EQQAELRPGRGHPEQPKHVTSSTSET*
        159 MUSIGHNPC
                                                                       (SEQ ID NO: 372)
                                    : EQQAELRPGKGNTEQPKQVTSSTSET*
         160 MUSIGHNPP
                                                                       (SEQ ID NO: 373)
 10
                                    : EQQAELKPGKGNTEQPKLITSSTSET*
                                                                       (SEQ ID NO: 374)
        161 MUSIGHNPE
                                    :TGQAELRPGRGAPEQGKKGKSSTSDR+
        162 A27635
                                                                       (SEQ ID NO: 375)
        163 MUSICHXW
                                    : QYQAELRPGKGTPRQQKKGKSSTS29*
                                                                       (SEQ ID NO: 376)
        164 MUSIGHIZA
                                   : QQQAVLRHGKGTHGQEKKGKSSTSES+
                                                                       (SEQ ID NO: 377)
         35 MUSIGHEH
                                    : QQQTXLGPGRGTPGQGRXGXSSTSGS+
                                                                       (SEQ ID NO: 378)
                                    : EQQAELRAGKGTPGQZKKGKSSVYFA+
        166 MUSIGHRH
                                                                       (SEQ ID NO: 379)
 15
        167 HV00$HOUSE
                                    : Eqqaelkagkgtpgqqkqgestrset+
                                                                       (SEQ ID NO: 380)
                                    :QQKAELAASKGTPGQEKKGRSSTSES*
        168 N$1P19H
                                                                       (SEQ ID NO: 381)
                                    : QQQTELRPGKGTPGQEKRGKSSHLRL*
                                                                       (SEQ ID NO: 382)
(SEQ ID NO: 383)
(SEQ ID NO: 384)
        169 MUSIGHZAD
                                    : EXVGGLQGSSFDPGKASKGTSQRAET+
        170 B30515
                                  : EQQADLKLGKGNPEQPKLATPSTSET+
        171 MUSIGHEB
                                  : eqvgglkpgkgtpdksdvkdnakset*
: dqqpdlkpssgspghpskstskttet*
        172 227889
                                                                       (SEQ ID NO: 385)
 20
        173 MUSIGHAAC
                                                                       (SEQ ID NO: 386)
                                  : DQQPDLKPSSGSPGMPSKSTSKTTET+
        174 HV61$MOUSE
                                                                       (SEQ ID NO: 387)
                                  : DQQPDLKPSSGSPGNPSKSTSKTAET+
        175 MUSIGVHR2
                                                                       (SEQ ID NO: 388)
                                  : Doopglkpssgspgnpskstskttet+
: Doopglkpssgspgnpskntskttet+
        176 PL0100
                                                                       (SEQ ID NO: 389)
                                                                       (SEQ ID NO: 390)
(SEQ ID NO: 391)
        177 MUSIGHAAO
        178 MUSIGHGA6
                                  : DQQPGLKPSSGSPGDPSKTTSKTTET*
                                   : DOOPGLEPSSSPGNPSKTTSKTTET*
 25
        179 MUSIGHJY
                                                                       (SEQ ID NO: 392)
                                    : DHOPGLKPSSGSPGNPSKNTSKTTET*
                                                                       (SEQ ID NO: 393)
(SEQ ID NO: 394)
        180 MUSIGHGAL
                                   : DOOPGLEPSSSPGNPSRSTSKTTET+
        181 MUSIGHOOK
                                    : DQQPGLKPSAGSPGNPSKSTSKTAET*
                                                                       (SEQ ID NO: 395)
        182 HV62$HOUSE
                                                                       (SEQ ID NO: 396)
(SEQ ID NO: 397)
                                    : POOPGLEPSSGSPGMPSESTSETS
        183 MUSIGHAAGA
        .84 MUSIGHGAS
                                    : DOOPGLEPSSGSPGNPSKNTSKTIET+
                                    : DOOPGLKPSSGSPGDPSKMTSKTPET+
 30
        185 MUSIGHGA4
                                                                       (SEQ ID NO: 398)
                                    : BOOPSLEPSSGSPGNPSKSTSKTTET*
        186 MUSIGHAGI
                                                                       (SEQ ID NO: 399)
                                    : DOOPGLEPSSGSPGNPSKHTSETTET*
        187 PL0102
                                                                       (SEQ ID NO: 400)
                                    : DQQPGLKPSSGSPGNPSKNTSETTIT*
        188 HV46SMOUSE
                                                                       (SEQ ID NO: 401)
                                    : ZOOPSLKPSSGSPGNPSKSTSKTSET*
        189 MUSIGHZT
                                                                       (SEQ ID NO: 402)
                                    : POOPSLKPSSGSPGNPSKSTSRTTET*
        190 MUSICHACD
                                                                       (SEQ ID NO: 403)
 35
                                    : POOPSLICPSSGSPGNPSXSTSXTAET+
        191 MUSIGHAGO
                                                                       (SEQ ID NO: 404)
                                    : DQQPDLKPSSGFPGNPSKSTSKTTET*
        192 MUSIGAM32
                                                                       (SEQ ID NO: 405)
                                    : POOPSLKPSSGSPGKPSKSTSKTNET*
        193 MUSIGRAFY
                                                                       (SEQ ID NO: 406)
                                    : EQQPSLEPSSGSPGNPSKSTPKTSET*
                                                                       (SEQ ID NO: 407)
        194 MUSIGRAGE
                                    : EQQPSLXPSSGSPGNPSKSTSTTSET*
                                                                       (SEQ ID NO: 408)
        195 MUSIGHAGE
                                    : EQQLSLKPSSGSPGNPSKSTSKTTET+
        196 MUSIGHAGE
                                                                       (SEQ ID NO: 409)
                                    :QQQPGLEPSPGPPGEPSQSTSETTET*
. 40
                                                                       (SEQ ID NO: 410)
        197 MUSICHAAM
                                   : QQKPGLAPSGSPGKSTKSNSKQTDT*
                                                                       (SEQ ID NO: 411)
        198 HV43$MOUSE
                                  *TOTOXXKRAARARGESEGAARARGESE
        199 MUSICHUVI
                                                                       (SEQ ID NO: 412)
                                    :QQXPGLAPSSGSPGKSAMSNSKQTOT*
                                                                       (SEQ ID NO: 413)
        200 MUSIGHAZI
                                    : COKPGLAPSEGSPGKSALSHSKOTDT.
                                                                       (SEQ ID NO: 414)
        201 MUSIGHBP
                                    : QQKPGLQPSSGSPGKAAISNSKQSHT*
                                                                       (SEQ ID NO: 415)
        202 MUSIGHZZA
                                   : QOKPGLOPSSGSPGKAAISNSKQANT*
 45
                                                                       (SEQ ID NO: 416)
        203 MUSIGMUV2
                                    *QCXPVLAPSGSPGKSAMSHSKQLDT*
                                                                       (SEQ ID NO: 417)
        204 AJ2456
                                   :QQKPSLQPSSDSPGKAAMSNSKQADT*
                                                                       (SEQ ID NO: 418)
        205 MUSICHMB
```

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HUMAN HEAVY CHAIN SURFACE PATCHES

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```
(SEQ ID NO: 419)
                                   : ERVGDLEPGRGIPGKAPKGDSKKIET.
           1 HUMIGHVS
                                                                      (SEQ ID NO: 420)
                                   : ERVGDLEPERGIPGKAPKGDSKKIET*
           2 HUMIGHVR
                                                                      (SEQ ID NO: 421)
5
           3 H36005
                                    : EQVGGLKPGRGTPGKAPKGDSKKTET*
                                                                      (SEQ ID NO: 422)
                                    : EQVGGLQPGKGTSGKASKGDSKKTET.
           4 PL0122
                                                                      (SEQ ID NO: 423)
            HV3D$HUMAN
                                    : EQLGGLQPGRGTPGKBSKGDSKRAET*
                                                                      (SEQ ID NO: 424)
                                    : EQLGGLQPGRGTPGKDSKGNSKRAET*
           6 HUNIGHAT
                                                                      (SEQ ID NO: 425)
                                    : EQLGGLQPGRGTPGKDSRGNSKRAET*
             B34964
                                                                      (SEQ ID NO: 426)
                                   : EQVGGLQPGRGTPGKDSKGNSKRAET*
             A34964
10
                                   : EQVGGLQPGRGTPGKDSKGNAKRAET.
                                                                      (SEQ ID NO: 427)
             PL0123
                                                                      (SEQ ID NO: 428)
          10 HVJFSHUMAN
                                    : EQVGGLQPGRGTPGKDSKGDSRRAET*
                                                                      (SEQ ID NO: 429)
                                    : EQVGGLQPGRGTPGKDSKGNSRRAET*
          11 JL0048
                                                                      (SEQ ID NO: 430)
                                    : QQVGGLEPGRGTPGKDSKGBSKRAET*
             HV3B$HUMAN
                                                                      (SEQ ID NO: 431)
                                    : EQLGDLQPGRGTPGKASKGNSKRAET*
          13
            HUMIGHBV
            HV3E$HUMAN
                                    : EQVGGLQPGRGTTGKDSKGDSKRAET*
                                                                      (SEQ ID NO: 432)
          14
                                                                      (SEQ ID NO: 433)
                                    : QQVGGVQPGRGTPGRDSRGNSKRAET*
15
             PL0116
          15
          16
             HV3K$HUMAN
                                    : QQVGGVQPGRGIPGKDSKGNSKRPET+
                                                                      (SEQ ID NO: 434)
                                    : EQVGGVQPGRGIPGXDSKGDSKRPET*
                                                                      (SEQ ID NO: 435)
          17
            N$2PB4H
                                                                      (SEQ ID NO: 436)
                                    : QQVGGVQPGRGTPGKDSHGDSKRPET*
          18
             HV3I$HUMAH
                                    :QKVGGVQPGRGTPGKDSKGHSKRTET*
                                                                      (SEQ ID NO: 437)
          19
             HV3JSHUMAN
                                    : QEVGGVZPGRGTPGKBSKGBSKRAET*
                                                                      (SEQ ID NO: 438)
          20 HV3GSHUMAN
                                                                      (SEQ ID NO: 439)
                                    : POLGGLOPGRGTPGKDSNGDSKQAZT*
20
          21 HVOHSHUKAN
                                                                      (SEQ ID NO: 440)
                                    : EQLGGLQPGRGSPGKDTHGDSKEAZT*
          22
             HV3O$HUNAN
                                                                      (SEQ ID NO: 441)
                                    : AQLGGLQPGRGTPGKDSHGDSKQAZS*
          23 HV3NSHUMAN
                                    : POLGGLOPGRGTPGKVSQGDSKQAZT*
                                                                      (SEQ ID NO: 442)
          24 HV3R$HUMAN
                                                                      (SEQ ID NO: 443)
                                    : EQVGGLQPGRGTPGKVSQGDSKEPIT*
          25 HV3PSHUMAN
                                    : POLGGLOPERGTPGKESKGNSHRAET*
                                                                      (SEQ ID NO: 444)
          26 HUNIGHCY
                                    : EQVGDLQPGRGBPGKDSKGNAKRVET+
                                                                      (SEQ ID NO: 445)
          27 HVJTSHUNAN
25
                                                                      (SEQ ID NO: 446)
                                    : EQVGDLQPGRGNPGKDSKGNAQRPET*
          28 HVJUSHUKAN
                                    :QQVGGVQPGRGTLGKDSKGNSKRAET+
                                                                      (SEQ ID NO: 447)
          29
            PL0098
                                    :QZVGGAZPGRGSPGKASKGBSKRAET+
                                                                      (SEQ ID NO:
                                                                                   448)
          30 HV3HSHUMAN
                                                                      (SEQ ID NO: 449)
                                    : QQVGGLKPGRGSPGKDSKGNAQRTZT*
          31 HV3ASHUKAN
                                    : DOVGGLEPGRGTPGKKSKGDSKTPET*
                                                                      (SEQ ID NO: 450)
             HVJSSHUMAN
          32
                                                                      (SEQ ID NO: 451)
                                    : BOLGGLOPGRGTSREDSKGNSKRAET*
          33 HUNIGHAW
30
                                                                           ID NO: 452)
                                    : EQVGALQPGRGTPGKDSQADSKEAZT+
                                                                      (SEQ
          34 HV3Q$HUMAE
                                    : EQLGGLQPGRGTPGK----VEGSVET*
                                                                      (SEQ ID NO: 453)
          35 A36040
                                                                      (SEQ ID NO: 454)
                                    : ECVGAFOPGRGMSGKASKGDSKRPDT*
          36 HUMIGHAM
                                                                      (SEQ ID NO:
                                    : EQVGAPQPGKGNSGKASKGDSKRPDT*
                                                                                   455)
          37 HUMIGHAO
                                                                      (SEQ ID NO: 456)
                                    : EQVGAPQPGKGHSGKASKGDSHRPDT*
          38 HUNIGHAR
                                                                      (SEQ ID NO: 457)
                                    : QQVGGVQAGRANPGKDSRGISKRTET*
35
          39
             HVILSHUMAN
                                    : QQVAEVRPGKGTPGQQKQGESTRSET*
                                                                      (SEQ ID NO: 458)
          40 HVLASHUMAN
                                                                      (SEQ ID NO: 459)
                                    : QQVAEVRPGRGTPGQQRQGTSTRSET*
          41 A32483
                                    : QQVAEVKPGKGTPGQQKQGTSARSET*
                                                                      (SEQ ID NO: 460)
          42 HUNIGHAY
                                                                       (SEQ ID NO: 461)
                                    : QQVAEVKPGKGTPGQQKQGTSIRSDT*
          43 HUNIGHCU
                                    : QQVAEVEPGEGTFGQEEQGTSIRSDT*
                                                                       (SEQ ID NO: 462)
          44 HUNIGHBS
                                                                       (SEQ ID NO: 463)
                                    : QQVAEVRPGRGTPGQQNQGTSTRSDT*
40
          45 HUMIGVHLS
                                    : QQVGEVKPGRGTPGQQXQDTSTRSDT*
                                                                      (SEQ ID NO: 464)
          46 HUMIGHBY
                                                                       (SEQ ID NO: 465)
(SEQ ID NO: 466)
                                    : QQVAEVXPGRGTPGHPRQGASFRSDS*
          47 HV1C$HUMAN
                                    : QQVSELKPGKGTPGQQGTGTSVKART*
          48 H34964
                                                                       (SEQ ID NO: 467)
                                    : ZQVAEVKPGKGSPGKPSQGKSIKAST*
          49 HUMIGHCY
                                                                       (SEQ ID NO: 468)
                                    : EQVAEVXPGRGSPGKPSQGKSIKAST*
          50 PL0119
```

	51 HV1F\$HUMAN	:QQVAEVKPGRGDPGRPRQASSTISAT+	(SEQ ID NO: 469	9)
	52 D34964	: eqvaevpqgkgrpgkslqgkslkast+	(SEQ ID NO: 476	oj.
	53 HV1D\$HUMAN	: QQMAEVKPGRGTPGKPGVVPSPPSET*	(SEQ ID NO: 47:	1)
	54 HV1ESHUMAN	: QQVAEVKPGRGTPGRYIWEPSFFNEG*	(SEQ ID NO: 472	2)
5	55 JL0047	:QQQAGLKPSSGSPGKPSKSTSKTAAT*	(SEQ ID NO: 47:	•
	56 HUMIGHBW	:QQQPGLKPSSGSPGKPSKSTSKTAAT*	(SEQ ID NO: 474	•
	57 E34964	: QQQPGLKPSSGSPGKPSKSTSNTAAT*	(SEQ ID NO: 475	•
	58 HUNIGHCW	:QQQPGLKPSSGSAGKPSKSTSKTAAT*	(SEQ ID NO: 476	•
	59 HV2FSHUMAN	:ROOPGLKPSSGPPGKPSRGTSRSAAT*	(SEQ ID NO: 477	,
	60 HV2ISHUMAN	: QQQAGLKPSSGSPGRTSKSTSKTAAT*	(SEQ ID NO: 478	•
10	61 HV2G\$HUMAN	: QQEPGLRPSSGTPGRTPRSTSKTAAT*	(SEQ ID NO: 479	•
	62 NSJFABH	: xqepglrpssgspgrtprstsktaat•	(SEQ ID NO: 480	•
	63 PS0091	: QQQPGLKPSSGSPSRVSKSTSKTPET*	(SEQ ID NO: 481	•
-	64 HUMIGHDA	: Qhqaglkrssgppgkpststsktaat*	(SEQ ID NO: 482	2)
	65 A26555	: Zqesglkptsgspgkpsksrskada*	(SEQ ID NO: 483	3)
	66 HVZESHUMAN	: QTKPTLKPTTGSPGRPSKSTSKDPVT•	(SEQ ID NO: 484	ı į
15	67 HV2D\$HUMAN	: QTKPTLKPTTGSPGKPSRSTSRDPVS*	(SEQ ID NO: 485	5
	68 A36005	: etrpalkptigspgktskttskopvt*	(SEQ ID NO: 486	
	69 HV2H\$HUMAN	: QNRPALKATTGSPGKTSETTSKDPAT*	(SEQ ID NO: 487	7)
	70 HV2A\$HUMAN	: QTTPALKPKTGSPGKTSRTDSKNPVT+	(SEQ ID NO: 488	3)
	71 HV2C\$HUNAN	: QTRPALRPTTGSPGEASETTSKGPGT*	(SEQ ID NO: 489)
	72 HV2B\$HUNAN	: QTRPALKPTIGSPGKTSETTSRDTAY*	(SEQ ID NO: 490))
20	73 JL0049	: Legvqlwggrgisrkyakgngkrdes+	(SEQ ID NO: 491	1)

EXAMPLE 2

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DETAILED DESCRIPTION OF METHOD FOR CONSTRUCTING THREE-DIMENSIONAL MODEL OF ANTIBODY VARIABLE REGION

[0070] The references cited in the text below are listed at the end of this Example.

[0071] The first antibody Fab structure was determined in 1972. Since then, no more than about twelve Fab structures have been published, a number that represents a very small fraction of the total antibody repertoire (>108 antibodies). To understand the molecular basis of this antibody diversity will require knowledge of either a large number of x-ray structures, or the rules by which combining site topography is governed. The development of such prediction rules has now reached the point where variable regions of antibodies can be modelled to an accuracy approaching that of the medium resolution x-ray structure.

[0072] The interaction of an antibody with its cognate antigen is one of the most widely accepted paradigms of molecular recognition. To understand the antibody-antigen interaction in atomic detail requires knowledge of the three-dimensional structure of antibodies and of their antigen complexes. Traditionally such information has come from x-ray crystallographic studies (see Davies et al. for review (Davies et al., 1988)).

[0073] The modelling of antibody combining sites was first attempted by Padlan & Davies (Padlan et al., 1976) at a time when very few antibody structures were known. Nonetheless, Padlan and colleagues recognized that the key lay in high structural homology that existed within the β-sheet framework regions of different antibody variable domains. The antigen combining site is formed by the juxtaposition of six interstrand loops, or CDRs (Complementarity Determining Regions) (Kabat et al., 1987), on this framework. If the framework could be modelled by homology then it might be possible to model the CDRs in the same way. Padlan and Davies (Padlan et al., 1976) reasoned that CDR length was the important determinant of backbone conformation though the number of antibody structures was insufficient to thoroughly test this maximum overlap procedure (MOP). This notion was not picked up again until the early 1980's when Pedersen and Rees proposed a similar approach to modelling antibody combining sites based on a more extensive analysis of antibody structures (de la Pas et al., 1986).

[0074] Those essentially knowledge-based procedures are best exemplified for antibodies by the work of Chothia & Lesk (Chothia et al., 1986) who, in 1986, extended and modified the MOP procedure by introducing the concept of "key" residues. These residues allow the further subdivision of CDRs of the same length into "canonical" structures which differ in having residues at specified positions that, through packing, hydrogen bonding or the ability to assume unusual values of the torsion angels φ, ψ and ω, determine the precise CDR conformation (Chothia et al., 1989). Similar knowledge-based methods have been proposed for predicting loop conformations in general (Thornton et al., 1988; Tramontano et al., 1989). These methods rely on the crystallographic database of protein structures. However, none of the above knowledge-based methods has been totally successful. In particular, the MOP or canonical structure approaches have succeeded in modelling only five of the six CDRs. This stems from the fact that the third CDR of the

heavy chain, H3, is more variable in sequence, length and structure than any of the other CDRs.

[0075] To deal with this problem several groups have attempted to use ab initio methods to model the combining site (Bruccoleri and Karplus, 1987). The requirement with such methods is that the total allowable conformational space accessible to a particular CDR is sampled. Typical of purely geometric approaches is that of Go & Sheraga (Go and Sheraga, 1970) and more recently Palmer & Sheraga (Palmer and Sheraga, 1991), where the problem is reduced to one in which the central region of the polypeptide backbone, having characteristic bond length and bond angles, is constructed between the end points of the loop (CDR if an antibody loop) by a "chain closure" algorithm. In a modification of this algorithm, Bruccoleri & Karplus (Bruccoleri and Karplus, 1987) introduced an energy minimization procedure which greatly expanded the domain of conformational space searched during the chain closure procedure. This modification is incorporated into the conformational search program CONGEN (Bruccoleri and Karplus, 1987), which also allows the user to choose any set of standard bond length and bond angels such as the CHARMM (Brooks et al., 1983) standard geometry parameter sets. Other approaches such as minimization (Moult and James, 1986), or molecular dynamics (Fine et al., 1986) either fail to saturate conformational space or are unable to deal with the problem of long CDRs. Whichever of the ab initio methods is employed however, the problem is one of defining the selection criteria in such a way as to allow the unambiguous identification of the correct structure (in this context correct is defined by reference to an appropriate X-ray structure) within the ensemble of candidates, for every CDR. To date this has not been possible.

[0076] Recently a more holistic approach has been taken to the modelling of CDRs which combines the advantages of knowledge-based and *ab initio* methods in a single algorithm known as CAMAL (Combined Algorithm for Modelling Antibody Loops) (Martin et al., 1989; Martin et al., 1991). Previously this algorithm has been used to model individual CDRs in the presence of the crystal structure conformations of the other five. As is demonstrated below, CAMAL is able to predict the backbone conformations of all six CDRs of the antibody combining site to an accuracy approaching that of medium resolution x-ray structures. In addition the algorithm includes a procedure for selecting and fitting together the light and heavy chain framework regions prior to generation of CDR conformations, thus making possible the prediction of the entire variable region. Furthermore a new Monte Carlo (MC) simulated annealing method has been developed for the determination of sidechain conformations.

The Framework Region

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[0077] Antibody framework regions consist of conserved β-strands that form the β-barrel structure characteristic of immunoglobulin V-type regions. In the procedure described here each V-region is built from a database of known antibody structures, using sequence homology for selection of the light (L) and heavy (H) chain V-domains. The two domains are then paired by least squares fitting on the most conserved strands of the antibody β-barrel (Table 2 and Figures 5 & 6). The strand orientations were determined by analyzing the barrels of known antibody crystal structures.
 35 Eight antibodies were analyzed using a multiple structure fitting program as follows. Seven structures were fitted onto

one of the set selected at random and mean coordinates were calculated. All eight structures were then fitted onto these mean coordinates and new mean coordinates determined. This procedure was iterated until the mean coordinate set converged (5-10 cycles). The variance for the mean coordinates at each barrel point $(N,C\alpha,C)$ was calculated. In Figure 5 this variance is plotted against the projected positions of these points onto the conjugate axis of the barrel.

[0078] Strand 8 and all but two residues of strand 7 in both light and heavy chains were eliminated as they showed deviations greater than 3 σ (standard deviation units) from the mean coordinates. These two strands comprised the takeoff points of CDR H3, and suggests that any knowledge-based prediction of CDR H3 would have to account not only for sequence and length variation in the CDR itself, but also for the position of the participating strands. The remaining mean coordinates were used as a scaffold onto which the L and H chains were fitted. Strands 7 and 8 in the final framework were obtained from the database structure used in the construction. The framework strands are marked + in the multialignment in Table 2.

[0079] The sidechains were then replaced using a 'maximum overlap' method, in which sidechain templates were fitted on backbone atoms with the sidechain torsion angles being adjusted to match those of equivalent torsions in the parent sidechain.

The Combining Site

[0080] The procedure for predicting the structure of combining sites combines a database search with a conformational search procedure. The architecture of the program suite to perform this task is outlined in Figure 7.

[0081] The database search utilizes distance constraints for each of the six CDR loops determined from known antibody structures. These constraints were determined by calculating $C\alpha$ - $C\alpha$ distances within known loops and using a search range of $\underline{x} + 3.5\sigma$ (the mean ± 3.5 standard deviation units). A database containing all the proteins in the Brookhaven Protein Databank (Bernstein et al., 1977) is then searched for fragments which satisfy the constraints for

a loop of the required length. The middle section of the loop is then deleted and reconstructed using the conformational search program CONGEN (Bruccolen and Karplus, 1987). For loops of six or seven residues, the structure database appears to saturate the conformational space available to the backbone adequately and only sidechains are built by conformational search. Loops shorter than six residues are built by conformational search alone since this is computationally feasible and the number of loops selected from the database becomes unacceptably large as loop length decreases.

[0082] When modelling a complete combining site, loops of 6 or more residues are modelled individually with the other loops absent. If the loops are built consecutively, small errors can accumulate leading to a poor result (Martin, 1990). All the loop conformations are then evaluated using a solvent modified potential, which excludes the attractive van der Waals and electrostatic terms of the non-bonded energy function contained within the GROMOS (Aqvist et al., 1985) potential. The lowest five energy conformations are selected and filtered using a "structurally determining residue" algorithm (FILTER), based on backbone torsion angles observed in the original database loops. Since the database search is not used for the shortest loops of 5 residues or fewer, the FILTER algorithm cannot be used. Energy is thus the only available selection criterion and the short loops are built last, in the presence of the longer loops.

Side Chains

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[0083] The determination of sidechain positions was previously done using the iterative sidechain determination algorithm described by Bruccoleri et al. (Bruccoleri and Karplus, 1987). Unfortunately the CHARMM (Brooks et al., 1983) force field fails to select the correct conformations of exposed hydrophobic sidechains. There is no penalty for having an exposed uncharged atom, without solvent present. CONGEN is also unable to saturate the conformational space for a large number of sidechains (more than 6 residues).

[0084] Recently Lee et al. (Lee and Levitt, 1991; Lee and Subbiah, 1991) has proposed a method for searching conformational space for a large number of sidechains using MC simulated annealing. A simple energy function is used for the evaluation of conformations generated by a biased random walk:

$$E = \sum_{i=1}^{n} \epsilon_{o} \left(\left(\frac{r_{o}}{r} \right)^{6} - 2 \left(\frac{r_{o}}{r} \right)^{12} \right) + \kappa_{o} \cdot COS(3\omega)$$

Where the first term is a simple *Lennard-Jones* potential which evaluates the non-bonded contacts between the atoms in a given molecule, the second term is a simple torsional term which only applies to C-C bonds. The torsional term biases the function towards 60° rotamers. ε_0 and κ_0 are constants. The metropolis function:

$$P = C^{\frac{-\delta E}{T}}$$

is used to evaluate the energy function. Any move which results in a decrease in energy is accepted, and any move which results in a positive δE is only accepted with the probability P. This simple method can be used to search the large conformational space defined by a set of torsion angles in amino-acid sidechains, and find or define the global minimum which exist for a set of sidechains. T is the simulation temperature.

[0085] When searching sidechain conformations using this method the simulation system usually gets trapped in an energetic minima well before the global minimum is encountered, at a high temperature, without the solution space having been searched sufficiently. This problem can be solved by truncating the *Lennard-Jones* potential, thus allowing atoms to pass through each other. In reality this function would converge towards infinity when the distance *r* between the atoms approaches zero.

[0086] The evaluation of sidechain conformations generated is done solely on the basis of energy, for internal (core) residues, since good van der Waal's interactions are considered to be equal to a good packing of the sidechains. The situation becomes more complicated when trying to predict the conformation of surface residues. The lowest van der Waal's interaction is obtained by a combination of sidechain conformations which minimize the overlap of atoms, this means that the lowest energy is obtained with extended conformations of sidechains, without considering good packing of sidechains.

[0087] Using the fact that hydrophobic, bulky residues will be shielded by the hydrophilic sidechains, and will be buried in the surface, it is possible to generate a simple function which will evaluate these macroscopic observations. These functions can either be implemented in the objective evaluation function of the Monte Carlo simulation, or as is

done here, added as a post processing step. Including an accessibility/hydrophobicity term in the evaluation function would slow down the calculation considerably, hence the term has been added as a post processing function. The function used is a sum of the product of relative exposed surface area multiplied by the residual hydrophobicities. The hydrophobicities used are taken from Cornette et al. (Cornette et al., 1987).

$$f_{conformation} = \sum_{i=1}^{n} -A_{irel} \cdot H_{irel}$$

n is the number of sidechains reconstructed. The surface area is calculated using the tesselated icosahedron approach (Chau and Dean, 1987), which is not very precise (0.1 percent), but is able to evaluate a large number of conformations. The function is evaluated for the final 2,000 conformations and the lowest value conformation selected as the best. [0088] Using this simple approach it is possible to integrate over a large phase space with many degrees of freedom, and get a complete sampling of the space.

Predicted Structures of an Anti-hapten, Anti-peptide and Two Anti-protein Antibodies

[0089] In the following section the predicted structures of four different antibody F_v regions are presented and ana-- lyzed. The antibodies are:

- Gloop-2 (Darsley and Rees, 1985), an anti-lysozyme antibody whose Fab structure was determined by Jeffrey et al., (Jeffrey et al., 1991) and which was used as a learning exercise during the development of CAMAL.
- D1.3 (Amit et al., 1986), an anti-lysozyme antibody whose uncomplexed F_v coordinates were supplied by R. Poljak
 et al. after the model coordinates had been deposited.
- 36-71 (Rose et al., 1990), an anti-phenylarsonate antibody whose Fab structure was carried out by D. R. Rose, et al., and whose coordinates were obtained after the model coordinates had been deposited.
- 3D6 (Grunow et al., 1988), an anti-protein (GP41 of HIV) antibody whose Fab structure was carried out by D. Carter et al. (Carter, 1991) and whose coordinates were obtained after the model coordinates had been deposited. For this antibody, the model was generated using the canonical loop method of Chothia & Lesk (Chothia et al., 1989; Chothia et al., 1986) for CDRs L1, L2, H1 and H2, while L3 and H3, which cannot be modelled using canonical structures, were constructed using CAMAL.

[0090] All four models were subjected to both restrained and unrestrained energy minimization using the DISCOVER (TM Biosym Technology) potential with 300 cycles of steepest descents, followed by conjugate gradient minimization until convergence to within 0.042J (0.01 Kcal) occurred.

[0091] The resolution and R-factors of the x-ray structures are given in Table 3 together with the parent frameworks selected in building the models. The structures and models were compared by global fits of the loops. The β -barrel strands 1 to 6, as described above, were least squares fitted and the RMS deviation was then calculated over the loops. The backbone (N,C α ,C) RMS values for fitting model and crystal structure frameworks were between 0.4 and 0.9x10⁻¹⁰m (0.4 and 0.9 Å), illustrating the conservation of the core β -barrel. Using all eight strands RMS deviations between 0.6 and 1.2x10⁻¹⁰m (0.6 and 1.2 Å) were observed.

[0092] Global fits (Table 4) give a more realistic measure of the accuracy of the model than a local least-squares fit over the loops since they account for the overall positioning of the loops in the context of the F_v structure. Local fits, which give lower RMS deviations, are also shown in Table 4. Differences between local and global RMS deviations arise from differences in V_H/V_L domain packing and differences in loop 'take off' angles and positions.

[0093] Table 5 shows the canonical loops selected from modelling 3D6. Backbone structures of the modelled CDRs, superimposed on the x-ray structures after global fitting are shown in Figure 8. General features and points of interest for each of the six CDRs are discussed below.

Analysis of the CDR Regions

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[0094] During the comparison of CDR conformations in the V-region models and the x-ray Fab structures it was observed that at certain positions in a CDR, the peptide backbone may adopt either of two conformations by undergoing

a "peptide flip" (1,4 shift). This phenomenon is also seen in type 2 β -turns (Paul et al., 1990). Dynamics simulations of β -turns show that the transformation energy between $\phi 1 = -00$, $\psi 1 = -30$, $\phi 2 = -90$, $\psi 2 = 0$ and $\phi 1 = -00$, $\psi 1 = 120$, $\phi 2 = 90$, $\psi 2 = 0$ has a maximum value of 5 kcal (Paul et al., 1990). This is low enough to allow selection of either conformation. The peptide flip is observed within several canonical classes (as described by Chothia et al. (Chothia et al., 1989)) and the hydrogen bonding pattern used to determine the conformation of a canonical class does not disallow the peptide flip. Any modelling procedure should therefore take these, or any other multiple conformations, into consideration where the transformation energies are sufficiently low to permit population of the different conformational forms. Table 6 shows an example of the "peptide-flip" phenomenon from the crystallographic database of antibody structures. It should be noted that a single crystal structure will not show multiple conformations since the crystallization will 'freeze out' one of the conformations. During the modelling procedure the two populations of conformers are easily extracted from a set of ab initio generated loops, by using a torsional clustering algorithm.

CDR-L1

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[0095] In Gloop-2 and D1.3, all five low energy conformations were very similar with RMS deviations differing by less than 0.25x10⁻¹⁰m (0.25 Å) (backbone) and 0.35x10⁻¹⁰m (0.35 Å) (all atoms). The FILTER algorithm was unable to distinguish between the conformations and the lowest energy structure was selected.

[0096] Although CDR-L1 of 3D6 was originally built using the canonical loop from HyHEL-10, the midsection was rebuilt by conformational search, for the following reason. HyHEL-10 and REI CDR-L1 loops are placed in the same canonical ensemble (Chothia et al., 1989) although they contain a 1-4 shift (peptide flip) relative to one another between the fifth and eighth residues of the loop (residues 28-31) (see Table 6).

[0097] 36-71 shows the same 1-4 shift between the model and crystal structure CDRs. Both crystal structure and model were compared with other loops of the same canonical class as defined by Chcthia et al. (Chothia et al., 1989). It was found that the hydrogen bonding pattern which determines the conformation was conserved.

CDR-L2

[0098] CDR-L2 of D1.3 has two adjacent threonines (49, 50) which in the x-ray structure are packed against the tyrosine at the fourth position of CDR-H3, thus minimizing the exposed hydrophobic sidechains. In the unminimized model the threonine sidechains are exposed to the solvent, but after energy minimization, this packing is observed.

CDR-L3

[0099] In Gloop-2, D1.3 and 36-71 the proline at the seventh position in the loop is correctly predicted in the *cis* conformation. It has previously been suggested that the conformation of CDR-L3 is dictated by the presence of a proline in position 8 or 9 (Chothia et al., 1989) within the loop. 3D6 does not have a proline in either position. Only 7 out of 290 CDR-L3 sequences (Kabat et al., 1987) lack a proline at both positions and in all of the published x-ray structures this proline is present. This is an example of a situation where either a new canonical class may need to be defined or where the canonical rule breaks down altogether, and an alternative method must be employed.

[0100] The 3D6 L3 loop is 7 residues in length and was built using database loops alone where conformational space is saturated by means of fragments selected from the crystallographic database (Global RMS 2.01x10⁻¹⁰m (2.01 Å), N,Cα,C), and by using CAMAL (Construction: Q[Q(YNS)Y]S, Global RMS: 1.97x10⁻¹⁰m 1.97 Å, N,Cα,C). The similarity of the structures generated by the two procedures illustrates the utility of the database search and suggests that, for shorter loops it is capable of saturating the available conformational space.

CDR-H1

[0101] Using the Kabat and Wu definition of CDR-H1 places this loop as an extension of the β -sheet. The extended nature of this stretch of peptide limits its conformational flexibility and CDR-H1 is generally modelled accurately (Martin et al., 1989; Chothia et al., 1989).

[0102] In Gloop-2 and D1.3, the Phe or Tyr sidechain at the second position in the loop is poorly placed and packs against Leu at the penultimate position in HFR1 (see Table 2). 36-71 has a well-placed Asn at this position, rather than the more common bulky hydrophobic sidechain.

55 CDR-H2

[0103] CDR-H2 of 36-71 is similar in sequence to F19.9 (Strong et al., 1991), (36-71: YNNPGNGYIA (SEQ ID NO: 492); F19.9: YINPGKGYLS (SEQ ID NO:493)). While the structurally determining residues specified by Chothia and

Lesk (Chothia et al., 1989) are conserved, the backbone conformations are different: F19.9 has a bulge at the -PGN-Gly, compared with 36-71, giving the loop a 'kink' in the middle. The model of 36-71 shows a 1-4 shift, though the sidechains are still well placed.

[0104] In Gloop-2, the all atom RMS deviation is poor $(3x10^{-10}\text{m})$ $(3.00 \, \text{Å})$ (Jeffrey et al., 1991) when compared with the P2₁ crystal structure, owing to rotations of the Phe at position 3 in the loop and Tyr at position 10 by approximately 120° about the χ_2 torsion angle. Gloop-2 has been solved in two different crystal forms, P2₁ and P1 (Jeffrey et al., 1991; Jeffrey, 1989). When compared with the P1 structure, the sidechains are placed almost perfectly and the all atom RMS (global fit) drops to 2.23x10⁻¹⁰m (2.23 Å).

[0105] This concerted sidechain motion between crystal forms illustrates the effects of crystallization conditions on surface sidechain placement. Even though surface sidechains may show low temperature factors indicating low mobility in the crystal, their mobility in solution may be high. In the Gloop-2 P1 structure, the mean sidechain temperature factor for the F_v domain is 13.46 (σ = 8.20) while the sidechains of these two residues of H2 show mean temperature factors of 5.56 (σ = 0.68) for the Phe at position 3 and 7.10 (σ = 1.73) for the Tyr at position 10.

5 CDR-H3

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[0106] CDR-H3 is the most variable of the six CDR's with all lengths up to 21 residues being represented in Kabat et al., (Kabat et al., 1987). This extreme variability results from V-D-J splicing (Schilling et al., 1980) and has always been a problem when attempting to model antibodies. Such loops may be divided into short (up to 7 residues), medium (up to 14 residues) and long (15 or more residues). Using the CAMAL procedure, short and medium CDR-H3's can be modelled as accurately as other CDR's of similar lengths. Although long CDR-H3's are more difficult and cannot, at present, be built to the same accuracy, the chain trace is still correct.

[0107] It is unlikely that the longer loops consist of 'pure' loops (i.e., all random coil or turn). In crystal structures of antibodies with medium to long CDR-H3 loops (McPC603 (Rudikoff et al., 1981): 11 amino acids (aa); KOL (Marquart et al., 1980): 17 aa; F19.9 (Lascombe et al., 1989): 15 aa) the loops consist of a disordered β-sheet extension from the β-barrel core and a 5-8 residue random coil/turn connecting these two strands.

[0108] To determine the nature of medium to long loops (>8 residues) which satisfy the CDR-H3 constraints, a complete search of the Protein Databank for loops of length 8-20 residues, was performed using the inter-Cα distance constraints determined from known antibody crystal structures for CDR-H3. The resulting loops were then analyzed using the DSSP (Kabsch and Sander, 1983) program, which is able to assign secondary structure to polypeptide structures. The amount of secondary structure for each length of loop was calculated, and it was observed that for loops longer than 12 residues the amount of secondary structure within each of the classes described in DSSP was constant. The number of loops selected is also constant (approximately 150 loops) for loops longer than 12 residues. A closer inspection of each of the length ensembles shows indeed that the loops are the same between the groups.

[0109] This analysis shows that, like the long CDR-H3 crystal structures, the selected fragments consist of β-strands connected by 5-8 residue loops. For loops above 12-13 residues in length, the same loops are selected, but with extensions to the β-strands. This is called the "sliding-ladder" effect. In addition, the maximum size of a random coil or turn fragment in any of the structures contained in the Protein Databank tends not to exceed 8 residues, as determined by DSSP. This implies that the conformational space of longer loops is not saturated by the database and, although it is unlikely that long loops in antibodies will differ significantly from long loops in other structures, confidence in the prediction must be correspondingly reduced.

[0110] By how much is the usefulness of the CAMAL algorithm reduced by this observation?

[0111] The frequency of occurrence of different CDR-H3 lengths in antibody sequences described by Kabat et al. (Kabat et al., 1987) was analyzed. Figure 10 shows that more than 85% of H3 loops have lengths between 4 and 14 residues which can be modelled accurately by the CAMAL algorithm.

[0112] CDR-H3 of D1.3 is of average length (8 residues), though no loops of this length are seen in the available antibody structures. The crystal structure coordinate set showed an RMS of 1.9x10⁻¹⁰m (1.9 Å) compared with the model.

[0113] The 36-71 loop is 12 residues long. The conformation is correctly predicted as a short loop connecting an extension of the β -sheet.

[0114] The 3D6 H3 loop is 17 residues long. While KOL (Marquart et al., 1980) has the same length it has only one residue in common with 3D6 and only one conservative mutation. There is thus no reason to believe that the conformations would be similar. The final predicted conformation of 3D6 is an extended β -sheet, as in the crystal structure. The difference between the predicted and the crystal structure of 3D6-H3 is due to a twist of 5-7° in the extended β -sheet loop (see Figures 9A-9D). Such a twist has also been observed for complexed and uncomplexed antibodies by Wilson et al. (Wilson and others). This suggests that long CDR-H3 loops may be flexible and actively involved in antigen binding.

The Complete Variable Region

[0115] Prediction of the strand positions and $V_L^-V_H$ orientation in the framework β-barrel was exact for all of the four antibodies. The backbone (N,Cα,C) RMS deviations from the crystal structures were between 0.56 and 0.86x10⁻¹⁰m (0.56 and 0.86 Å), despite the fact that, in all cases the V_L and V_H regions of a particular model were derived from different antibody structures. This suggests that this method will do well in procedures such as humanization (German et al., 1991), where correct framework positioning is important. The backbones of all six CDRs in all four antibodies are essentially correctly predicted, as shown in Figure 8. There are two important points to make about these predictions. First, the position of each CDR on its framework barrel is correct. Thus, CDR-framework interactions can be confidently monitored. The only deviation from the x-ray structure is CDR-H3 of antibody 3D6 which has been previously discussed. Second, the all atom RMS deviation between models and x-ray structures is dominated by sidechain positions. In most instances this deviation is due to a small number of incorrectly positioned, exposed sidechains (for example, in D1.3 the only sidechains which are incorrectly predicted are Tyr 9 of L1, Trp 4 of L3, Tyr 2 of H1 and Tyr 4 of H3). Since each CDR is constructed in the absence of other CDRs, the force field may choose a rotamer which is 120° away from that found in the crystal structure. This effect has also been observed by Lee et al. (Lee and Levitt, 1991).

Conclusion

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- [0116] For antibodies having CDR H3 regions of 14 residues or less the complete variable domain can be modelled to an accuracy approaching that of medium resolution x-ray structures. For antibodies with longer H3 loops the CAMAL algorithm is likely to need an additional procedure in which molecular dynamics simulations are also incorporated.

 [0117] The canonical approach of Chothia et al. appears to work well (at least in modelling backbones) where it may
 - [0117] The canonical approach of Chothia et al. appears to work well (at least in modelling backbones) where it may be applied and may be used successfully in combination with the CAMAL procedure.
- [0118] One important observation that has emerged from these studies is that a given loop can exist in several conformations. In particular, this seems likely for CDR-L1 and, to a lesser extent, CDR-L3 and longer CDR-H3's. A simple combinatorial calculation shows that, if each of these three loops can exist in three separate conformations, a given combining site can have 3³ = 27 different topographies. Clearly, this would explain the origins of cross reactivity and would allow for induced fit of antigens.

5	Table 2: Alignment of antibody sequences used in the modelling. indicates β -strand regions used in the fitting for modelling framewo strands is (H or L - Chain) - FR(Framework region)-(Strand numone of the heavy chain becomes HFR1.	gloop-2 d13 3671 3D6	gloop-2 d13 3071 3D6	gloop-2 dj3 3671 3De Anlibody	Antibody gloop-3 d13 3671 3D0
	Alignm 3-stran (H or heavy	- u =	514	SE SE	SEQ ID NO
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15	intibody s ns used in ain) - FR becomes I	7		TOUR	DIQMTQSPSS DIQMTQSPSS DIQMTQSPSS
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25	used in th g for model ork region)	D Z Z X X X X X X X X X X X X X X X X X	X C D D D D D D D D D D D D D D D D D D		DRVS-ITC
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40	Table 2: Alignment of antibody sequences used in the modelling. '*' indicates CDR, indicates β -strand regions used in the fitting for modelling frameworks. Nomenclature strands is (H or L - Chain) - FR(Framework region)-(Strand number), thus for example one of the heavy chain becomes HFR1.		**************************************		+ 2 2 2 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4
45	regions; '+' for β -barrel mple strand	**************************************	. 000 . 000	* * * * * * * * * * * * * * * * * * *	+000+ · · · · · · · · · · · · · · · · ·
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Table 3:

Details of the antib		_		
			Framew	ork Model
Antibody	Resolution	R-factor	Light	Heavy
Gloop-2	2.80	ution R-factor Light	HyHEL-5	
D1.3	_	-	REI	NEW
36-71	1.90	20.9	Gloop2	NEW
3D6	2.70	17.7	REI	KOL

							-	-			
					RMS local	ocal (A)			RMB	(V) 1340	
Antibody	CDR	requence	SEQ ID NO	Co	N,Co,C	VII CO	All MC	Co	N.Co.C All CO	Au co	All MC
2000	:	BASIOFESTOLVES		0.73	0.71	2.08			0.17	2.00	-
		RASICIANNIVIA	0 5	2.39		4.34	9.	2.73	3.68	1.0	4.53
36-71		BASIOCOLNING	96	2.71	2.49	1.00	4.89	20.02	3.31	6.1.0	8.67
		BACOCIONINI	101	3	3 2		3		0.78	2.2	
300		Was Alexander									
Gloop-3	S	AASTLDS	•	0.28	0.29	0. 8 0	1.00	9.0	0.0	1.10	1. 10
DLJ	1	YITITLIAID	190	0.67	0.73			0.5	1.03	2.01	
36-71		FIT(SRS)OIS	800	0.64	•	3.84	2.28	0.73	0.73	3.15	3.40
3D6		KASSLES	108	0.41	0.43	1.37	1.20	0.83	0.00	1.78	1.80
Closes.	;	LOWIESVAPILT	803	0.0	o 5	1.73	:	0.78	0.74	9	1.10
D1.3	(OHIF WST) PIRT	503	1.41	1.36	2.00). :	1.76	1.78		J.20
30-71		QQIQ(NAL)PIRT	504	1.00	1.00	2.24	2.10		1.30	2.27	3.30
3D6		Q Q(YNS)Y S	808	-	1.88	8.04	3.90	2.31	1.07	2.20	3.8
Gless-3	=	Tregari	50 6	0.80	0.70	2.08	-6	1.08	1.01	3.04	2.00
D1.3		וס(אסע)או	807	0.1	0.43	2.33	2.00	0.88	0.00	8.24	3.91
36-71		S(NOI)N	508	0.0	0.88	2.22		1.04	0.97	2.61	2.23
306		DYAMH	809	0.67	0.77	1.62	1.11	0.2	0.72	7.69	1.20
Gloss.3	3	EIIF(PON)SIKTY	810	0.65	•	-	1.70	1.20	0.0	2.2	3.10
01.3		MIW(GDG)NITO	511	0.43	0.43	1.88	1.00	0.87	0.00	-	- 60
30-71		YNNIP(QNQ)YIIA	813	9.0	0.78	2.01	3.30	1.47	1.41	1.79	
3D6		DISSSOMSI	813	0.45	0.82	2.88	2.03	0.98	0.00	2.60	2.10
Gloop-2	H	IR(EIR)Y	514	0.00	9.0	3.0	3	0.07	1.07		
01.3		EN(D(YNL)D)Y	516	0.38	0.83		6.30	1.26	0.01		1.88
36-71		SEYY(O(OSY)K)PDY	. 516	1.98	1.78	1.10	4.00	2.00	2.88		9
300		GROYY[D(SGG)YF]TVAPDI	317	3.66	3.42	5.93	4.01	4.30	3.98	9.30	8.30

calculating the RMS over the loops. The total RMS of the frameworks (N,C α ,C) is 0.81, 0.60, 0.86 and 0.56 respectivly calculated by least-squares fitting the conserved core of the two structures upon each other and difference between model and crystal structure loop coordinates. The RMS values are a global fit =construction area, ()= Chain closure, all sidechains are constructed. RMS(Root Mean Square) Table 4: Sequence and conformational search construction scheme for each of the 24 CDRs,

Loop	Canonical	Sequence	SEQ ID NO
Li	HyHEL-10	RASQSISRWLA	518
	(3D6)	RASQSIGNNLH	497
L2	REI	EASNDLA	519 ·
	(3D6)	KASSLES	501
H1	McPC603	DFYME	520
	(3D6)	DYAME	509
H2	KOL	I I WD DG S DQ""	521
	(3D6)	ISWDSSSIG	513

Table 5: Canonical loops selected for the model of 3D6(taken from Chothia et al (1989)).

Table 6

				laIa	able 6:			
1	Backbone ¢				•	d REI classified otide flip are ind		nonical group
	Residue	Number .	24	25	26	27	28*	29*
5	REI	Sequence φ/ψ	Q -/138	A -103/157	S -96/7	Q -158/142	S -40/108	I 112/9
	HyHEL-10	Sequence φ/ψ	R -/108	A -85/135	S -88/64	Q 172/160	S -64/-38	I 9/63
	Residue	Number	30*	31*	32	33	32	
)	REI	Sequence φ/ψ	l 79/-77	K -146/21	Y -104/89	L -143/133	N -144/-	SEQ ID NO: 522
	HyHEL-10	Sequence φ/ψ	G -63/107	N 85/-15	N -105/12	L -129/118	H -126/-	SEQ ID NO: 518

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sized Loops in Proteins. Proteins: Struct., Funct., Genet. 6, pp. 382-394. [0158] "Wilson, I. et al., Presented at Structure and Function Meeting in Honour of Sir David Phillips, 1-3 July, 1991, Oxford, UK. 5 SEQUENCE LISTING [0159] GENERAL INFORMATION 10 (i) APPLICANT: PEDERSEN, Jan T. SEARLE, Stephen M.J. REES, Anthony R. ROGUSKA, Michael A. GUILD, Braydon C. 15 (ii) TITLE OF INVENTION: SURFACE RESIDUE VENEERING OF RODENT ANTIBODIES (iii) NUMBER OF SEQUENCES: 522 20 (iv) CORRESPONDENCE ADDRESS: (A) ADDRESSEE: Sughrue, Mion, Zinn, Macpeak & Seas (B) STREET: 2100 Pensylvania Avenue, N.W. (C) CITY: Washington 25 (D) STATE: D.C. (E) COUNTRY: United States (F) ZIP: 20037-3202 (v) COMPUTER READABLE FORM: 30 (A) MEDIUM TYPE: Floppy disk (B) COMPUTER: HP 9000/700 Workstation (C) OPERATING SYSTEM: UNIX (D) SOFTWARE: In house 35 (vi) CURRENT APPLICATION DATA: (A) APPLICATION NUMBER: 07/942,245 (B) FILING DATE: 09-SEP-1992 (C) CLASSIFICATION: 40 (ix) TELECOMMUNICATION INFORMATION: (A) TELEPHONE: (202) 293-7060 45 ~(B) TELEFAX: (202) 293-7860 (C) TELEX: 6491103 (1) INFORMATION FOR SEQ ID NO:1 50 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 109 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 55 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

	Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly 1 10 15	
5	Glu Arg Val Ser Leu Thr Cys Arg Ala Ser Gln Glu Ile Ser Gly T 20 25 30	yΈ
10	Leu Ser Trp Leu Gln Gln Lys Pro Asp Gly Thr Ile Lys Arg Leu I 35 40 45	le
15	Tyr Ala Ala Ser Thr Leu Asp Ser Gly Val Pro Lys Arg Phe Ser G 50 55 60	lу
	Arg Arg Ser Gly Ser Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Se 65 70 75	er 30
20	Glu Asp Phe Ala Asp Tyr Tyr Cys Leu Gln Tyr Leu Ser Tyr Pro Le 85 90 95	au
25	Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala 100 105	
	(2) INFORMATION FOR SEQ ID NO:2	
. 30	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 109 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
35	(ii) MOLECULE TYPE: peptide	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:	

	Asp 1	Ile	Gln	Met	Thr 5	Gln	Ser	Pro	Ala	Ser 1		Ser	Ala	Ser		Gly L5
5	Glu	Thr	Val	Thr 20	Ile	Thr	Cys	Arg	Ala 25		Gly	Asn	Ile	His 3	Asn O	Tyr
10	Leu	Ala_	Trp 35	Tyr	Gln	Gln	Lys	Gln 40		Lys	Ser	Pro	Gln 4	Leu 5	Leu	Val
15	Tyr	Tyr 50	Thr	Thr	Thr	Leu	Ala 55		Gly	Val	Pro	Ser 6		Phe	Ser	Gly
	Ser 65	Gly	Ser	Gly	Thr	Gln 70	Tyr	Ser	Leu	Lys	Ile 75	Asn	Ser	Leu	Gln	Pro 80
20	Glu	Asp	Phe	Gly	Ser 85	Tyr	Tyr	Cys	Gln	His 90		Trp	Ser	Thr	Pro	Arg
25	Thr	Phe	Gly	Gly 100	Gly	Thr	Lys	Lev	1 Gli 10!		e Ly	/s Ar	rg Ai	rg		

(3) INFORMATION FOR SEQ ID NO:3

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 107 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

	Asp 1	Ile	Val	Leu	Thr 5	Gln	Ser	Pro	Ala	Ile 1		Ser	Ala	Ser	Pro	Gly 5
5	Glu	Lys	Val	Thr 20	Met	Thr	Cys	Ser	Ala 25		Ser	Ser	Val		Tyr 0	Met
10	Tyr	Trp	Tyr 35	Gln	Gln	Lys	Ser	Gly 40		Ser	Pro	Lys		Trp 5	Ile	Tyr
15	Asp	Thr 50	Ser	Lys	Leu	Ala	Ser 55		Val	Pro	Val		Phe 0	Ser	Gly	Ser
	Gly 65	Ser	Gly	Thr	Ser	Tyr 70	Ser	Leu	Thr	Ile	Ser 75	Ser	Met	Glu	Thr	Glu 80
20	Asp	Ala	Ala	Glu	Tyr 85	Tyr	Cys	Gln	Gln	Trp		Arg	Asn	Pro	Thr	Phe 5
25	Gly	Gly	Gly	Thr 100		Leu	Glu	Ile	Lys 105		, Ala	ı				
	(4) INF	ORMA [*]	TION F	OR SI	EQ ID I	NO:4										
30	(i)	SEQUE	ENCE	CHARA	ACTER	RISTIC	S:									
		(B) T	ENGTH YPE: a OPOLO	mino a	cid	acids										
35	(ii)	MOLE	CULE	TYPE:	peptid	е				•						
	(xi)	SEQL	ENCE	DESC	RIPTI	ON: SE	EQ ID I	NO:4:								
40	. Asp 1	Ile	Val	Leu	Thr 5	Gln	Ser	Pro	Ala	Thr 1		Ser	Val	Thr	Pro 1	Gly 5
45														-		

	Asn	ser	Val	Ser 20	Leu	Ser	Cys	Arg	Ala 2		Gln	Ser	Ile		Asn 80	Asn
5	Leu	His	Trp 35	Tyr	Gln	Gln	Lys	Ser 40		Glu	Ser	Pro	_	Leu 5	Leu	Ile
10	Lys	Tyr 50	Ala	Ser	Gln	Ser	Ile 55		Gly	Ile	Pro		Arg O	Phe	Ser	Gly
. 15	Ser 65	Gly	Ser	Gly	Thr	Asp 70	Phe	Thr	Leu	Ser	Ile 75	Asn	Ser	Val	Glu	Thr 80
	Glu	Asp	Phe	Gly	Met 85		Phe	Cys	Gln	Gln 9		Asn	Ser	Trp	Pro 9	Tyr 5
20	Thr	Phe	Gly	Gly 100	Gly	Thr	Lys	Leu	Glu 105		Lys	s Ar	g Ala	a		
	(5) INF	ORMA	TION F	FOR S	EQ ID	NO:5										
25	(i) :	SEQUI	ENCE	CHAR	ACTE	RISTIC	CS:		•							-
	,	(B) T	YPE: a	H: 108 imino a OGY: I		acids		-								
30	(ii)	MOLE	CULE	TYPE	: peptio	de										
	(xi)	SEQL	JENCE	DES	CRIPT	ION: S	SEQ ID	NO:5	:			-				
35	Glu 1	Ile	Val	Leu	Thr 5		Ser	Pro	Ala	Ile 1	-	Ala	Ala	Ser	Leu 1	Gly .5
40	Gln	Lys	Val	Thr 20	Ile	Thr	Cys	Ser	Ala 25		Ser	Ser	Val		Ser 0	Leu
45	His	Trp	Tyr 35	Gln	Gln	Lys	Ser	Gly 40		Ser	Pro	Lys		Trp 5	Ile	Tyr
	Glu	Ile 50	Ser	Lys	Leu	Ala	Ser 55		Val	Pro	Ala	Arg 6	Phe 0	Ser	Gly	Ser
50	Gly 65	Ser	Gly	Thr	Ser	Tyr 70	Ser	Leu	Thr	Ile	Asn 75	Thr	Met	Glu	Ala	Glu 80
	Asp	Ala	Ala	Ile	Tyr 85	Tyr	Cys	Gln	Gln	Trp	Thr O	Tyr	Pro	Leu	Ile 9	Thr 5
55		•														

Phe	Gly	Ala	Gly	Thr	Lys	Leu	Glu	Leu	Lys	Arg	Ala
			100					105			

(6) INFORMATION FOR SEQ ID NO:6

	(i) S	SEQUE	NCE C	HARA	CTERI	STICS	:									
10		(B) TY	NGTH: PE: an	nino ac	id	cids										
15	(ii)	MOLE	CULE T	YPE: p	eptide	ı										
15	(xi)	SEQU	ENCE	DESC	RIPTIO	N: SE	Q ID N	O:6:								
20	Glu 1	Ser	Val	Leu	Thr 5		Pro	Pro	Ser	Ala 1	_	Gly	Thr	Pro	_	Gln L5
	Arg	Val	Thr	Ile 20	Ser	Cys	Thr	Gly	Thr 25	_	Ser	Asn	Ile		Ser O	Ile
25	Thr	Val	Asn 35	Trp	Tyr	Gln	Gln	Leu 40		Gly	Met	Ala		Lys 5	Leu	Leu
30	Ile	Tyr 50	Arg	Asp	Ala	Met	Arg 55		Ser	Gly	Val		Thr 0	Arg	Phe	Ser
35	Gly 65	Ser	Lys	Ser	Gly	Thr 70	Ser	Ala	Ser	Leu	Ala 75	Ile	Ser	Gly	Leu	Glu 80
	Ala	Glu	Asp	Glu	Ser ,85	Asp	Tyr	Tyr	Cys	Ala 9		Trp	Asn	Ser	Ser	Asp 5
40	Asn	Ser	Tyr	Val 100	Phe	Gly	Thr	Gly	Thr 109		Val	Thr	Val	Leu 11		Gln
45	(7) INF	ORMAT	TION F	OR SE	Q ID N	10:7										
	(i)	SEQUE	NCE C	HARA	CTER	STICS	: :						*			
50		(B) T	NGTH PE: ar	nino ac	cid	cids										
	(ii)	MOLE	CULE 1	YPE: p	peptide											
55	(xi)	SEQU	ENCE	DESC	RIPTIC	N: SE	Q ID N	0:7:								

	Asp 1	Ile	Val	Met	Thr 5	Gln	Ser	Pro	Ser	Ser 1	Leu	Ser '	Val S	Ser A	la G 15	ly
5			•													
10	Glu	Arg	Val	Thr 20		Ser	Cys	Lys		Ser 5	Gln	Ser	Leu		Asn 30	Ser
	Gly	Asn	Gln 35		Asn	Phe	Leu	Ala 4		Tyr	Gln	Gln		Pro	Gly	Gln
15	Pro	Pro 50	Lys	Leu	Leu	Ile	Tyr 5		Ala	Ser	Thr		Glu io	Ser	Gly	Val
20	Pro 65	Asp	Arg	Phe	Thr	Gly 70	Ser	Gly	Ser	Gly	Thr 75	Asp	Phe	Thr	Leu	Thr 80
	Ile	Ser	Ser	Val	Gln 85		Glu	Asp	Leu	Ala 90		Tyr	Tyr	Cys		Asn 5
25	Asp	His	Ser	Tyr 100	Pro	Leu	Thr	Phe	Gly 10	Ala 5	Gly	Thr	Lys	Leu 13		Ile
30	Lys	Arg	Ala 115					•								
	(8) INF	ORMA	TION I	FOR S	EQ ID	NO:8										
35	(i)	SEQU	ENCE	CHAR	ACTEF	RISTIC	S:									
		(B) T	YPE: a	H: 103 amino a OGY: li	icid	acids										
40	(ii)	MOLE	CULE	TYPE:	peptid	le										
	(xi) SEQI	JENCE	DESC	RIPTI	ON: S	EQ ID	NO:8:								
45																

	Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln A 1 10 15	
5	Val Thr_Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly A 20 25 30	sn
10	His Val Lys Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu L 35 40 45	eu
15	The Phe His Asn Asn Ala Arg Phe Ser Val Ser Lys Ser Gly Ser S 50 55 60	er
	Ala Thr Leu Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp T 65 70 75	yr 80
. 20		
	Tyr Cys Gln Ser Tyr Asp Arg Ser Leu Arg Val Phe Gly Gly Thi	r
25	Lys Leu Thr Val Leu Arg Gln 100	
30	(9) INFORMATION FOR SEQ ID NO:9	
	(i) SEQUENCE CHARACTERISTICS:	
35	(A) LENGTH: 114 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:	

	Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly 1 5 10 15
5	Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser 20 25 30
. 10	Gln Gly Asn Thr Tyr Leu Arg Trp Tyr Leu Gln Lys Pro Gly Gln Ser 35 40 45
15	Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro 50 55 60
	Asn Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile 65 70 75 80
20	Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser 85 90 95
	Thr His_Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 105 110
25	Arg Ala
30	(10) INFORMATION FOR SEQ ID NO:10
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 109 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

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	As	p Il 1	e Gli	n Met	Thr 5		Thr	Thr	Ser	Ser		Ser	Ala	Ser		Gly 15
5	As	p Ar	g Val	l Thr 20		Ser	Cys	Arg	Ala 25	Ser (Gln .	Asp	Ile		Asn 0	Tyr
10	Le	u As	n Trg 3!		Gln	Gln	Lys	Pro 40		Gly :	Thr '	Val	Lys 4	Leu 5	Leu	Val
15	Тy	r Ty: 5		: Ser	Arg	Leu	His 55		Gly	Val I	Pro :	Ser 6	_	Phe	Ser	Gly
	Se:		y Ser	Gly	Thr	Asp 70	Tyr	Ser	Leu	Thr :	Tle : 75	Ser	Asn	Leu	Glu	His 80
20	Gl	u Asj	p Ile	Ala	Thr 85	Tyr	Phe	Cys	Gln	Gln (Gly :	Ser	Thr	Thr		Arg 5
?5	Th	r Ph	a Gly	Gly 100	Gly	Thr	Lys	Leu	Glu 105	Ile	Lys	Arg	Arg	I		
	(11) INF	FORMA	ATION F	OR SE	Q ID N	O:11										
	, (i) s	SEQUE	NCE C	HARAC	CTERIS	TICS:										
30		(B) T	PE: an	: 109 an nino aci GY: line	d	ids										
35	(ii)	MOLE	CULE T	YPE: p	eptide											
	(xi)	SEQU	ENCE	DESCR	IPTION	N: SEQ	ID NO): 11 :	-							
1 0	Asp 1		Gln	Met 1	Thr G 5	ln I	le P	ro Se	er Se	r Lev 10	. Sez	Àla	a Sei	. Lev	Gly 15	•
15	Asp	Arg	Val	Ser 1 20	lle S	er ¢	ys Ai	rg Al	La Se 25	r Gln	Asp	Ile	a Asr	n Asr 30	Phe	
	Leu	Asn	Trp 35	Tyr (Sln G	ln L	ys Pi	O As	p Gl	y Thr	Ile	Lys	Leu 45	ı Lev	lle	
50	Tyr	Phe 50		Ser A	arg S	er G	ln Se 55	er Gl	.y Va	l Pro		Arc	, Phe	Ser	Gly	

	Ser 65	Gly	Ser	Gly	Thr	Asp 70	Tyr	Ser	Leu	Thr	11e 75	Ser	Asn	Leu	Glu	Gln 80
5	Glu	Asp	Ile	Ala	Thr 85	Tyr	Phe	Cys	Gln	Gln 90	-	Asn	Ala	Leu	Pro 9	_
10	Thr	Phe	Gly	Gly 100	Gly	Thr	Lys	Leu	Glu 105		Lys	Arg	Ala			
	· (12) INF	ORMA	TION F	OR SE	EQ ID I	NO:12										
15	•	EQUE					:									
		(A) LE (B) TY (C) TO	PE: am	nino ac	id	cids										
20	(ii) N	MOLEC	ULE T	YPE: p	eptide											
	(xi)	SEQUE	ENCE	DESCF	RIPTIO	N: SE	Q ID N	O:12:								
25	Asp 1	lle	Gln	Met		Gln 5	Ser	Pro	Se:		r Lei 10	u Se	r Al	a Se	er Va	1 Gly 15
30	Asip	Arg	Val	Thr 20		Thr	Cys	Arg		a Sei 25	e Gli	n Se	r Il	.e Se	er Ar 30	g Trp
35	Leu	ı Ala	Trp 35	_	Gln	Gln	Lys		G1;	y Ly:	s Vai	l Pr	o Ly	s Le 45	u Le	u Ile
	Tyr	Lys 50		Ser	Ser	Leu		sei 5	Gl;	y Va	l Pr	o Se	ė0 ė0	g Ph	ne Se	r Gly
40	Ser 65		Ser	Gly	Thr	Glu 70		Thi	Le	u Th	r Il		r Se	r Le	eu Gl	n Pro 80
	Asp	Asp	Phe	Ala	Thr 89		Туг	Cys	s G 1:	n Gl	n Ty: 90	r As	n Se	r Ty	r Se	r Phe 95
45	Gly	y Pro	Gly	Th:	Ly:		l As	p Il				hr				
50	(13) INF	ORMA	TION F	OR SE	EQ ID I	NO:13										
	(i) S	EQUE	NCE C	HARA	CTERI	STICS	:									
55		(A) LE (B) TY (C) TO	PE: am	nino ac	id	cids		•								
	1 (ii)	MOLEC	ULE T	YPE: p	eptide											

5	Gln 1	Val	Gln	Leu	Gln 5		Ser	Gly	Thr	Glu 1		Ala	Arg	Pro	_	Ala 15
10	Ser	Val	Arg	Leu 20		Cys	Lys	Ala	Ser 2		Tyr	Thr	Phe		Thr 30	Phe
	Gly	Ile	Thr 35	Trp	Val	Lys	Gln	Arg 40		Gly	Gln	Gly		Glu 5	Trp	Ile
15	Gly	Glu 50	Ile	Phe	Pro	Gly	Asn 55		Lys	Thr	Tyr		Ala O	Glu	Arg	Phe
20	Lys 65	Gly	Lys	Ala	Thr	Leu 70	Thr	Ala	Asp	Lys	Ser 75	Ser	Thr	Thr	Ala	Tyr 80
	Met	Gln	Leu	Ser	Ser 85		Thr	Ser	Glu	Asp 9		Ala	Val	Tyr		Cys 5
25	Ala	Arg	Glu	Ile 100	Arg	Tyr	Trp	Gly	•							
30	(14) IN	FORM.														
35		(B) T	ENGTH YPE: a OPOLO	ımino a	acid	acids	3									
	(ii)	MOLE	CULE	TYPE	: pep _i ti	de										
40	(xi)	SEQL	JENCE	DES	CRIPT	ION: S	SEQ IC) NO:1	14:							
	Gln 1	Val	Gln	Leu	Lys 5		Ser	Gly	Pro	Gly 1		Val	Ala	Pro		Gln .5
45	Ser	Leu	Ser	Ile 20	Thr	Cys	Thr	Val	Ser 25		Phe	Ser	Leu		Gly 0	Tyr
50	Gly	Val	Asn 35	Trp	Val	Arg	Gln	Pro 40		Gly	Lys	Gly		Glu S	Trp	Leu
	Gly	Met 50	Ile	Trp	Gly	Asp	Gly 55		Thr	Asp	Tyr		Ser 0	Ala	Leu	Lys
55																

	Ser 65		Leu	Ser	Ile	Ser 70	Lys :	Asp A	sn S	er I	Lys So 75	er Gl	n Va	l Phe	Leu 80	
5	Lys	Met	Asn	Ser	Leu 1 85	His '	Thr i	Asp A	T qa	hr A 90	ala Ai	g Ty	т Туг	-	Ala 95	
10	Arg	Glu	Arg	Asp 100	Tyr	Arg	Leu		Tyr '		Gly			•		•
	(15) INF	ORMA	TION F	OR S	EQ ID I	NO:15										
15	()	EQUE					:						_			
		(A) LE (B) TY (C) TC	PE: an	nino ac	id	cids										
20	· (ii) ·	MOLEC	ULE T	YPE: p	eptide										-	
	(xi)	SEQUI	ENCE I	DESC	RIPTIO	N: SE	Q ID N	IO:15:								
? 5	Val 1		Leu	Gln	Gln	Ser	Gly	Ala	Glu	_	Met 10	Lys	Pro	Gly .	_	Ser 5
30	Val	Lys	Ile	Ser 20		Lys	Ala	Ser		Туг 5	Thr	Phe	Ser	Asp '		Trp
	Ile	Glu	Trp 35	Val	Lys	Gln	Arg	Pro 4		His	Gly	Leu	Glu 4		Ile	Gly
35	Glu	Ile 50	Lêu	Pro	Gly	Ser	Gly 5	_	Thr	Asn	Tyr	_	Glu O	Arg 1	Phe :	Lys
40	Gly 65		Ala	Thr	Phe	Thr 70		Asp	Thr	Ser	Ser 75	Ser	Thr	Ala '	lyr i	Met 80
4 5	Gln	Leu	Asn	Ser	Leu 85		Ser	Glu	Asp		Gly 0	Val	Tyr	Tyr (Cys 9	
	His	Gly	Asn	Tyr 100	_	Phe	e Ası	o Gly	7 Tr; 10:		Y					
50.	(16) INF	ORMA	TION F	OR S	EQ ID	NO:16										
	(i) S	SEQUE	NCE C	HARA	CTERI	STICS	3 :									
55		(B) TY	NGTH: PE: an POLO	nino ac	id	cids										

(ii) MOLECULE TYPE: peptide

5	Asp 1	Val	Gln	Leu	Gln 5		Ser	Gly	Pro	Ser 1		Val	Lys	Pro	Ser	Gln L5
10	Thr	Leu	Ser	Leu 20	Thr	Cys	Ser	Val	Thr 25	_	Àsp	Ser	Ile	_	Ser 0	Asp
	Tyr	Trp	Ser 35	Trp	Ile	Arg	Lys	Phe 40		Gly	Asn	Arg		Glu 5	Tyr	Met
15	Gly	Tyr 50	Val	Ser	Tyr	Ser	Gly 55		Thr	Tyr	Tyr	_	Pro O	Ser	Leu	Lys
20	Ser 65	Arg	Ile	Ser	Ile	Thr 70	Arg	Asp	Thr	Ser	Lys 75	Asn	Gln	Tyr	Tyr	Leu 80
	qsA	Leu	Asn	Ser	Val 85	Thr	Thr	Glu	Asp	Thr 9		Thr	Tyr	Tyr	Cys	Ala 5
25 .	Asn	Trp	Asp	Gly 100	Asp	Tyr	Trp	Gly								
30	(17) IN	FORM	ATION	FOR	SEQ II	D NO:	17									
	(i)	SEQUI	ENCE	CHAR	ACTE	RISTI	CS:									
35		(B) T	ENGTI YPE: a OPOL	mino :	acid	acids	i									
	(ii)	MOLE	CULE	TYPE	: pepti	de		•	•							
40	(xi)	SEQU	JENCE	DES	CRIPT	ION: S	SEQ ID	NO:1	7:							
	Glu 1	Val	Lys	Leu	Leu 5		Ser	Gly	Gly	Gly 1		Val	Gln	Pro	Gly	Gly L5
45	Ser	Leu	Lys	Leu 20	Ser	Cys	Ala	Ala	Ser 25		Phe	Asp	Phe		Lys 0	Tyr
50	Trp	Met	Ser 35	Trp	Val	Arg	Gln	Ala 40		Gly	Lys	Gly	Leu 4	Glu 5	Trp	Ile
55	Gly	Glu 50	Ile	His	Pro	Asp	Ser 55		Thr	Ile	Asn		Thr 0	Pro	Ser	Leu

	Lys 65	Asp	Lys	Phe	Ile :	Tle : 70	Ser :	Arg A	Asp A		la Ly 75	s As	n Se	r Le	u Ty:	
5	Leu	Gln	Met	Ser	Lys 1 85	Val i	Arg:	Ser (Glu A	.sp T) 90	nr Al	a Le	и Ту	r Ty	r Cys	5
10	Ala	Arg	Leu	His 100	Tyr	Tyr	Gly	Tyr	Asn 105	Ala 7	Cyr I	rp G	ly			
	(18) IN	FORM	ATION	FOR S	EQ ID	NO:18	3									
15	(i) :	SEQUE	ENCE (CHARA	CTER	ISTICS	S:									
		(B) T	ENGTH YPE: ar OPOLC	mino ad	cid	ıcids										
20	(ii)	MOLE	CULE .	TYPE:	peptide	e										
	(xi)	SEQL	JENCE	DESC	RIPTIC	ON: SE	Q ID I	NO:18:								,
25	Glu 1	Val	Gln	Leu	Val	Gln ;	Ser	c Gly	Gly		Val O	Val	Gln	Pro	_	Arg L5
30	Ser	Leu	Arg	Leu 20		Cys	Ser	Ser		Gly 5	Phe	Ile	Phe	_	Ser 10	туг
35	Ala	Met	Tyr 35	_	Val	Arg	Gln		Pro 0	Gly	Lys	Gly		Glu 5	Trp	Val
	Ala	Ile 50	Ile	Trp	Asp	Asp	_	/ Ser	' Asp	Gln	His		Ala O	Asp	Ser	Val
40	Lys 65		Arg	Phe	Thr	Ile 70		Arg	Asn	Asp	Ser 75	Lys	Asn	Thr	Leu	Phe 80
45	Leu	Gln	Met	Asp	Ser 85		Arg	Pro	Glu	Asp 9		Gly	Val	Tyr		Cys 5
	Ala	Arg	Asp	Gly 100		His	Gly	Phe	Cys 10		Ser	Ala	Ser	Cys 11		Gly
50	Pro	Asp	Tyr 115	Trp	Gly		•									
55	(19) IN	FORM	ATION	FOR S	EQ ID	NO:19)									
	(i)	SEQUI	ENCE (CHARA	CTER	ISTICS	S:									

(A) LENGTH: 113 amino acids

55					
	Leu Ser L	eu Thr Cys Thr 20	Val Ser Gl	y Thr Ser Phe 25	Asp Asp Tyr Tyr
50 .	Val Gln L	eu Glu Gln Ser 5	Gly Pro Gl	y Leu Val Arg 10	Pro Ser Gln Thr
	(xi) SEQUENC	CE DESCRIPTION: SE	EQ ID NO:20:		
45	(ii) MOLECULI	E TYPE: peptide			
40	(B) TYPE:	TH: 107 amino acids amino acid LOGY: linear			
	(i) SEQUENCE	E CHARACTERISTIC	S:		
35	(20) INFORMATIO	N FOR SEQ ID NO:20)		
	Gly		• •		
30	Tyr Cys A	la Arg Asn Tyr 100	Tyr Gly Se	r Thr Trp Tyr 05	Phe Asp Val Trp
	Leu Tyr Le	eu Gln Met Asn 85	Ala Leu Ar	g Ala Glu Asp 90	Thr Ala Ile Tyr 95
25	Ser Val Ly	ys Gly Arg Phe 70		r Arg Asp Thr 75	Ser Gln Ser Ile 80
20	Ala Ala Se 50	er Arg Asn Lys	Gly Asn Lys 55	s Tyr Thr Thr 6	Glu Tyr Ser Ala O
	-	35	40	- 3-, -1y	45
15	Tur Mat G			,	Leu Glu Trp Ile
	Ser Leu Ar	rg Leu Ser Cys 20		r Gly Phe Thr	Phe Ser Asp Phe
10	Glu Val Ly	ys Leu Val Glu 5	Ser Gly Gl	y Gly Leu Val	Gln Pro Gly Gly
	(xi) SEQUENC	E DESCRIPTION: SE	Q ID NO:19:		
5	(ii) MOLECULE	E TYPE: peptide			
•		amino acid LOGY: linear			

	Ser	THE	35	Val	ALY.	9111	PIO	40		wid	GIY	Dea		5	116	GIY
5	Tyr	Val 50	Phe	Tyr	His	Gly	Thr 55		Asp	Thr	Asp		Pro 0	Leu	Arg	Ser
o	Arg 65	Val	Thr	Met	Leu	Val 70	Asn	Thr	Ser	Lys	Asn 75	Gln	Phe	Ser	Leu	Arg 80
	Leu	Ser	Ser	Val	Thr 85	Ala	Ala	Asp	Thr	Ala 9		Tyr	Tyr	Cys		Arg 95
5	Asn	Leu	Ile	Ala 100	Gly	Cys	Ile	Asp	Val 105		o Gly	ł				
о	(21) IN	FORMA	ATION	FOR S	EQ ID	NO:2	1	•								
	(i) :	SEQUE	NCE	CHARA	CTER	RISTIC	S:									
:5	•	(B) TY	NGTH PE: ai	mino a	cid	acids										
	(ii)	MOLE	CULE T	TYPE:	peptid	le										
10	· (xi)	SEQU	ENCE	DESC	RIPTI	ON: S	EQ ID	NO:21	l:							
	Ġlu 1	Val	Lys	Leu	Asp 5		Thr	Gly	Gly	Gly 1	Leu 0	Val	Gln	Pro	Gly 1	Arg .5
:5 -	Pro	Met	Lys	Leu 20	Ser	Cys	Val	Ala	Ser		Phe	Thr	Phe	Ser 3	Asp 0	Tyr
10	Trp	Met	Asn 35		Val	Arg	Gln	Ser 40	Pro	Glu	Lys	Gly	Leu 4	Glu 5	Trp	Val
	Ala	Gln 50		Arg	Asn	Lys	Pro 55	Tyr	Asn	Tyr	Glu	Thr 6	Tyr o	Tyr	Ser	Asp
15	Sei 65	val	Lys	Gly	Arg	Phe 7.0	Thr	Ile	Ser	Arg	Asp 75	Asp	Ser	Lys	Ser	Ser 80
50	Va.	l Tyr	Leu	Gln	Met 85	Asn	Asn	Leu	Arg	Val 9	Glu O	Asp	Met	Gly	Ile	Tyr 5
	Tyn	r Cya	Thr	Gly 100		туг	туг	Gly	7 Met 105	: As _l	р Ту	r Tr	p Gl	У		
55	(22) IN	FORM	NOITA	FOR S	SEQ ID	NO:2	2									
	(i)	SEQUE	NCF (CHARA	ACTER	RISTIC	S:									

		(A) LE (B) TY (C) TC	PE: an	nino ad	cid	acids										
5	(ii)	MOLEC	ULE T	YPE:	peptid	е			٠							
	(xi)	SEQUI	ENCE	DESC	RIPTIC	ON: SE	EQ ID	NO:22	:							
10	Gln 1	Val	Gln	Leu	Lys 5		Ser	Gly	Ala	Glu 1	_	Val	Ala	Ala		Ser 15
15	Ser	Val	Lys	Met 20	Ser	Cys	Lys	Ala	Ser 2		Tyr	Thr	Phe	_	Ser 30	Tyr
	Gly	Val	Asn 35	Trp	Val	Lys	Gln	Arg 40	_	Gly	Gln	Gly	_	Glu 5	Trp	Ile
	Gly	Tyr 50	Ile	Asn	Pro	Gly	Lys 5		Tyr	Leu	Ser		Asn 0	Gļu	Lys	Phe
25	Lys 65	Gly	Lys	Thr	Thr	Leu 70	Thr	Val	Asp	Arg	Ser 75	Ser	Ser	Thr	Ala	Tyr 80
	Met	Gln	Leu	Arg	Ser 85		Thr	Ser	Glu	Asp 9		Ala	Val	Tyr		Cys 95
30	Ala	Arg	Ser	Phe 100	Tyr	Gly	Gly	Ser	Asp 10		Ala	Val	Tyr	Tyr 11		Asp
35	Ser	Trp	Gly 115										•			£
	(23) INF	ORMA	TION	FOR S	EQ ID	NO:2	3									
·40	(i) S	SEQUE	NCE C	HARA	CTER	ISTIC	S:									
45		(A) LE (B) TY (C) TO	PE: ar	nino a	cid	acids										
40	(ii) l	MOLEC	CULE 1	TYPE:	peptid	е										
	(xi)	SEQU	ENCE	DESC	RIPTIO	ON: SE	EQ ID	NO:23	: :							
50	Glu 1	Val	Gln	Leu	Gln 5		Ser	Gly	Val	Glu 10	Leu O	Val	Arg	Ala	Gly 1	Ser 5
55																

	Ser	Val	Lys	Met 20	Ser	Cys	Lys	Ala	Ser 2		Tyr	Thr	Phe		Ser 30	Asn
5	Gly	Ile	Asn 35	Trp	Val	Lys	Gln	Arg		Gly	Gln	Gly		Glu 5	Trp	Ile
10	Gly	Tyr 50	Asn	Asņ	Pro	Gly	Asn 55		Tyr	Ile	Ala		Asn 0	Glu	Lys	Phe
	Lys 65	Gly	Lys	Thr	Thr	Leu 70	Thr	Val	Asp	Lys	Ser 75	Ser	Ser	Thr	Ala	Tyr 80
15	Met	Gln	Leu	Arg	Ser 85	Leu	Thr	Ser	Glu	Asp 9		Ala	Val	Tyr	Phe 9	Cys 5
20	Ala	Arg	Ser	Glu 100	Tyr	Tyr	Gly	Gly	Ser 10		Lys	Phe	Asp	Ту г 11	Trp .0	Gly
	(24) IN	FORM	ATION	FOR:	SEQ II	D NO:	24									
25	(i)	SEQUI	ENCE	CHAR	ACTE	RISTIC	CS:									
		(B) T	ENGTI YPE: a OPOL	ımino a	acid	acids										
30	(ii)	MOLE				de										
		SEQL					SEQ ID	NO:2	4:							
35	Glu 1	Val	Gln	Leu	Val 5		Ser	Gly	Gly	Gly 10	_	Val	Gln	Pro	Gly .	
4 0 ·	Ser	Leu	Arg	Leu 20	Ser	Суз	Ala	Ala	Ser 25	_	Phe	Thr	Phe	Asn 3	Asp ' 0	Tyr
45	Ala	Met	His 35	Trp	Val	Arg	Gln	Ala 40		Gly	Lys	Gly	Leu 4		Trp '	Val
	Ser	Gly 50	Ile	Ser	Trp	Asp	Ser 55		Ser	Ile	Gly	Tyr 6		Asp	Ser '	Val
50	Lys 65	Gly	Arg	Phe	Thr	Ile 70	Ser	Arg	Asp	Asn	Ala 75	Lys	Asn	Ser	Leu '	Tyr 80
55	Leu	Gln	Met	Asn	Ser 85	Leu	Arg	Ala	Glu	Asp 90		Ala	Leu	Tyr	Tyr (

	Val	L Lys	Gly	Arg 100		Tyr	Tyr	Asp	Ser 10		Gly	Tyr	Phe		Val	Ala
5	Phe	a Asp	Ile 115	Trp	Gly	•										
10	(25) IN	FORM	ATION	FOR S	SEQ IE) NO:2	5									
	(i)	SEQU	ENCE (CHARA	ACTE	RISTIC	S:									
15		(B) T	ENGTH YPE: a: OPOLO	mino a	cid	acids						â				
	(ii)	MOLE	CULE	TYPE:	peptic	le										
20	(xi) SEQL	JENCE	DESC	RIPTI	ON: S	EQ ID	NO:25	5 :							
	Asp 1	Val	Leu	Met	Thr 5		Thr	Pro	Leu	Ser 1	-	Pro	Val	Ser	Leu 1	Gly 5
25	Asp	Gln	Ala	Ser 20	Ile	Ser	Cys	Arg	Ser 25		Gln	Ile	Ile	_	His O	Ser
30	Asp	Gly	Asn 35	Thr	Tyr	Leu	Glu	Trp		Leu	Gln	Lys		Gly 5	Gln	Ser
·35	Pro	Lys 50	Leu	Leu	Ile	Tyr	Lys 55		Ser	Asn	Arg		Ser O	Gly	Val	Pro
	Asp 65		Phe	Ser	Gly	Ser 70	Gly	Ser	Gly	Thr	Asp 75	Phe	Thr	Leu	Met	Ile 80
40	Ser	Arg	Val	Glu	Ala 85	Glu	Asp	Leu	Gly	Val	_	Tyr	Cys	Pḥe	Gln 9	
45	Ser	His	Val	Pro 100	His	Thr	Phe	Gly	Gly 105		Thi	: Lys	3 Lei	1 Gl	ı Ile	1
	(26) IN	FORM	ATION	FOR S	SEQ IC) NO:2	6									
50	(i)	SEQUI	ENCE (CHARA	ACTE	RISTIC	S:									
		(B) T	ENGTH YPE: a OPOLO	mino a	cid	acids										
55	(ii)	MOLE	CULE	TYPE:	peptic	le										
	4	١٥٥٥١	ITAIOT	DECC	DIDTI	ON. C	EO 10	NO.20	٠.							

_	Gln 1	Ser	Val	Leu	Thr 5	Gln	Pro	Pro	Ser		Ser O	Gly	Thr	Pro	_	Gln 15
5	Arg	Val	Thr	Ile 20		Cys	Ser	Gly	Thr 2		Ser	Asn	Ile		Ser 30	Ser
10	Thr	Val	Asn 35		Tyr	Gln	Gln	Leu 40		Gly	Met.	Ala		Lys 5	Leu	Leu
15	Ile	Tyr 50	Arg	Asp	Ala	Met	Àrg 55		Ser	Gly	Val	_	Asp 0	Arg	Phe	Ser
	Gly 65	Ser	Lys	Ser	Gly	Ala 70	Ser	Ala	Ser	Leu	Ala 75	Ile	Gly	Gly	Leu	Gln 80
20	Ser	Glu	Asp	Glu	Thr .85	Asp	Tyr	Tyr	Cys	Ala 9	_	Trp	Asp	Val		Leu 5
25	Asn	Ala	Tyr	Val 100	Phe	Gly	Thr	Gly	Thr 105	_	Va]	Thi	r Va.	l Lei		
	(27) INI	FORM	ATION	FOR:	SEQ II	O NO:	27									
30	(i) :	SEQUE	ENCE	CHAR	ACTE	RISTIC	CS:									
		-(B) T		mino a		acids										
35	(ii)	MOLE	CULE	TYPE	: pepti	de										
•	(xi)	SEQL	ENCE	DESC	CRIPT	ION: S	SEQ ID	NO:2	7:							
40	Gln 1	Val	Leu	Met	Thr 5	Gln	Thr	Pro	Ser	Ser	_	Pro	Val	Thr		Gly .5
	Gln	Gln	Ala	Ser 20	Ile	Ser	Суз	Arg	Ser 25		Gln	Ile	Ile		His O	Ser
45	Asp	Gly	Asn 35	Thr	Tyr	Leu	Glu	Trp		Leu	Gln	Lys		Gly 5	Gln	Ser
50	Pro	Lys 50	Leu	Leu	Ile	Tyr	Lys 55		Ser	Asn	Arg	Phe 6		Gly	Val	Pro
55	Asp 65	Arg	Phe	Ser	Gly	Ser 70	Gly	Ser	Gly	Thr	Ser 75	Phe	Thr	Leu	Ala	Ile 80
	•															

	Ser	Arg	Val	Glu	Ala 85	Glu	Asp	Glu	Gly	Val 9	Tyr o	Tyr	Cys	Phe	Glr	Gly 95
5	Ser	His	Val	Pro 100	His	Thr	Phe	e Gly	7 Gly 105		y Th	r Ly	s Le	u Gl 11		le
10	(28) INF	FORMA SEQUE														
15	,,	(A) LE (B) TY	:NGTH 'PE: ar		amino a											
	(ii)	MOLE	CULE .	TYPE:	peptid	е										
20	(xi)	SEQU	ENCE	DESC	RIPTIO	ON: SI	EQ ID	NO:28	3:							
	Asp 1	Val	Val	Met	Thr 5	Gln	Ser	Pro	Leu	Ser 1		Pro	Val	Thr		Gly L5
25	Gln	Pro	Ala	Ser 20	Ile	Ser	Cys	Arg	Ser 25		Gln	Ser	Leu	_	Tyr 0	Ser
30 .	Asp	Gly	Asn 35	Thr	Tyr	Leu	Asn	Trp 40		Gln	Gln	Arg		Gly 5	Gln	Ser
35	Pro	Arg 50	Arg	Leu	Ile	Tyr	Lys 55		Ser	Asn	Arg	Asp 6	_	Gly	Val	Pro
	Asp 65	Arg	Phe	Ser	Gly	Ser 70	Gly	Ser	Gly	Thr	Asp 75	Phe	Thr	Leu	Lys	Ile 80
40	Ser	Arg	Val	Glu	Ala 85	Glu	Asp	Val	Gly	Val 90		Tyr	Cys	Met		Gly 5
45	Thr	His	Trp	Ser 100	Trp	Thr	Phe	Gly	Gln 105		Thr	Lys	Val	Glu 11	Ile O	Lys
	(29) INI	FORMA	ATION	FOR S	EQ ID	NO:2	9									
50	(i) S	(B) TY	:NGTH 'PE: ar		amino a cid		S:									
55	(ii)	MOLE				e										
	/v:\	SEOU	, ENCE	DESC	DIDTI	ԴΝ - €!	בט וס	NO-20	1.							

5 .	Asp 1	Val	Leu	Met	Thr	Gln	Ser	Pro	Leu		Leu 0	Pro	[Va]	Thr	Leu	Gly 15
J	Gln	Pro	Ala	Ser 20		Ser	Cys	Arg	Ser 2		Gln	Ile	Ile	Ile	His 30	Ser
10	Asp	Gly	Asn 35	Thr	Tyr	Leu	Glu	Trp		Gln	Gln	Arg		Gly 45	Gln	Ser
15	Pro	Arg 50		Leu	Ile	Tyr	Lys 5		Ser	Asn	Arg	_	Ser 0	Gly	Val	Pro
	Asp 65	Arg	Phe	Ser	Gly	Ser 70	Gly	Ser	Gly	The	Asp 75	Phe	Thr	Leu	Lys	Ile 80
20	Ser	Arg	Val	Glu	Ala 85		Asp	Val	Gly	Val 9		Tyr	Cys	Phe		Gly 95
25	Ser	His	-Val	Pro 100		Thr	Phe	Gly	/ Gly 109		Thi	Ly:	s Va	1 G1 11		e
	(30) INF	ORMA	TION F	FOR S	EQ ID	NO:30)									
	(i) S	EQUE	NCE C	HARA	CTER	ISTICS	S:									
30		(B) TY	NGTH: PE: an	nino ad	cid	acids										
35	(ii) N	OLEC	ULE T	YPE:	peptid	θ										
	(xi) \$	SEQUE	ENCE	DESC	RIPTIO	ON: SE	Q ID I	NO:30	:							
40	Asp . 1		Val	Met	Thr 5		Ser	Pro	Asp	Ser 10		Ala	Val	Ser		Gly 5
45	Glu	Arg _.	Ala	Thr 20		Asn	Cys	Lys	Ser 25		Gln	Ser	Val	Leu 3		Ser
	Ser	Asn	Asn 35	Lys	Asn	Tyr	Leu	Ala 40		Tyr	Gln	Gln		Pro 5	Gly	Gln
50	Pro	Pro 50	Lys	Leu	Leu	Ile	Tyr 55		Ala	Ser	Thr	Arg 60		Ser	Gly	Val
55	Pro 65	Asp	Arg	Phe	Ser	Gly 70	Ser	Gly	Ser	Gly	Thr 75	Asp	Phe	Thr	Leu	Thr 80

	Ile	Ser	Ser	Leu	Gln 85	Ala	Glu	Asp	Val		Val 0	Тут	Туг	Cys	Gln	Gln 95
5	Tyr	Asp	Thr	Ile 100		Thr	Phe	Gly	Gly 10		Thr	Lys	Val		Ile 10	Lys
10	(31) IN	FORM	ATION	FOR	SEQ IC) NO:3	31									
	(i)	SEQUI	ENCE	CHAR	ACTE	RISTIC	CS:									
15	·	(B) T	ENGTI YPE: a	mino a		acids										
	(ii)	MOLE	CULE	TYPE	peptio	de										
20	(xi) SEQL	JENCE	DES	CRIPTI	ION: S	EQ ID	NO:31	l:		•	٠.				
25	Asp 1	Val	Leu	Met	Thr 5	Gln	Thr	Pro	Asp	Ser 10		Pro	Val	Ser		Gly .5
	Asp	Arg	Ala	Ser 20	Ile	Ser	Cys	Arg	Ser 25	_	Gln	Ile	Ile		His O	Ser
30	Asp	Gly	Asn 35	Thr	Tyr	Leu	Glu	Trp		Leu	Gln	Lys		Gly 5	Gln	Ser
35	Pro	Lys 50	Leu	Leu	Ile	Tyr	Lys 55		Ser	Asn	Arg	Phe 6	_	Gly	Val	Pro
40	65	Arg				70					75					80
•	Ser	Arg	Val	Glu	85	Glu	Asp	Leu	GIÅ	90 90	. –	TYE	Cys	Pne	_	Gly 5
45	Ser	His	Val	Pro 100	His	Thr	Phe	Gly	Gly 105		The	Lys	s Lei	1 Glu		ž
	(32) IN	FORM	ATION	FOR	SEQ II	Э NO:	32									
50	(i)	SEQU	ENCE	CHAR	ACTE	RISTIC	CS:									
55		(B) T	ENGTI YPE: & OPOL	amino a		acids										
		MOLE														
	(xi) SEQI	JENCE	E DESC	CRIPT	ION: S	EQ ID	NO:32	<u>?:</u>							

	Asp 1	Val	Gln	Leu	Val 5	Glu	Ser	Gly	Gly	Gly 10	_	Val	Gln	Pro		Gly 15
5	Ser	Arg	Lys	Leu 20	Ser	Cys	Ala	Ala	Ser 25		Phe	Thr	Phe	_	Ser O	Phe
10	Gly	Met	His 35	Trp	Val	Arg	Gln	Ala 40		Glu	Lys	Gly		Glu 5	Trp	Val
15	Ala	Tyr 50	Ile	Ser	Ser	Gly	Ser 55		Thr	Ile	Tyr	His 6		Asp	Thr	Val
	Lys 65	Gly	Arg	Phe	Thr	Ile 70	Ser	Arg	Asp	Asn	Pro 75	Lys	Asn	Thr	Leu	Phe 80
20	Leu	Gln	Met	Thr	Ser 85	Leu	Arg	Ser	Glu	Asp 90	_	Ala	Met	Tyr		Cys 5
25	Ala	Arg	Met	Arg 100	Lys	Gly	Tyr	Ala	Met 10		Tyr	Trp	Gly	Gln 11		Thr
	Thr	Val	Thr 115	Val	Ser								•			
30	(33)	NFOR	MATION	I FOR	SEQ I	D NO:	33									
	(i)) SEQU	JENCE	CHAR	RACTE	RISTI	CS:									
35		(B)	LENGT TYPE: TOPOL	amino	acid	acids		•			•					
40	(ii	i) MOL	ECULE	TYPE	: pepti	de	•									
	(x	(i) SEQ	UENC	E DES	CRIPT	ION: S	SEQ ID	NO:3	3:							
45	Glu 1	Val	_GIn_	Leu	Val 5		Ser	Gly	Gly	Gly 1		Val	Gln	Pro	Gly	Arg 15
	Ser	Leu	Arg	Leu 20	Ser	Cys	Ser	Ser	Ser 2	Gly 5	Phe	Ile	Phe	Ser 3	Ser 10	Tyr
50	Ala	Met	Tyr 35	Trp	Val	Arg	Gln	Ala 40		Gly	Lys	Gly	Leu 4	Glu 5	Trp	Val
55	Ala	Ile 50	Ile	Trp	Asp	Asp	Gly 5		Asp	Gln	Ris	Tyr	Ala 0	Asp	Ser	Val

	Lys 65	Gly	Arg	Phe	Thr	Ile 70	Ser	Arg	Asn	Asp	Ser 75	Lys	Asn	Thr	Leu	Phe 80
5	Leu	Gln	Met	Asp	Ser 85		Arg	Pro	Glu	Asp 9		Gly	Val	Tyr		Cys 95
10	Ala	Arg	Asp	Gly 100		His	Gly	Phe	Cys 109		Ser	Ala	Ser	Cys 11		Gly
	Pro	Asp	Tyr 115	Trp	Gly	Gļn	Gly	Thr 120		Val	LThi	va:	1 Se:			
15	(34) INF	ORMA	TION F	OR SE	EQ ID	NO:34							-			•
	(i) S	EQUE	NCE C	HARA	CTERI	STICS) :			-						
?0		(A) LEI (B) TYI (C) TO	PE: am	nino ac	id	cids										
?5		MOLEC SEQUE					Q ID N	IO:34:						,		
30	Glu 1	Val	Gln	Leu	Val 5		Ser	Gly	Gly	Gly 1	_	Val	Gln	Pro		Arg .5
35	Ser	Leu	Arg	Leu 20	Ser	Cys	Ala	Ala	Ser 25	_	Phe	Ile	Phe	Ser 3	_	Phe
	Gly	Met	His 35	Trp	Val	Arg	.Gln	Ala 40		Gly	Lys	Gly	_	Glu 5	Trp	Val
10		Tyr . 50	Ile	Ser	Ser	Asp	Gly 55		Thr	Ile	Tyr	His 6	_	Asp	Ser	Val
4 5	Lys 65	Gly_	_Yrđ	Phe	Thr	Ile 70	Ser	Arg	Asp	Asp	Pro 75	Lys	Asn	Thr	Lèu	Phe 80
	Leu	Gln	Met	Thr	Ser 85	Leu	Arg	Ser	Glu	Asp 90		Ala	Met	Tyr		Cys 5
50	Ala	Arg	Met	Arg 100	Lys _.	Gly	Tyr	Ala	Met 105		Tyr	Trp	Gly	Gln 11	Gly 0	Thr
55	Thr	Val	Thr 115	Val	Ser											
	(35) INF	ORMA'	TION F	OR SE	מו ח	NO:35										

(i) SEQUENCE CHARACTERISTICS:

_			'PE: aı	mino a	cid											
5		(0) 10	OPOLO	GY: lir												
	(ii)	MOLE	CULE .	TYPE:	peptid	le										
10	(xi)	SEQU	ENCE	DESC	RIPTI	ON: S	EQ ID	NO:35	ō:							
	Gln 1	Val	Gln	Leu	Val 5	Glu	Ser	Gly	Gly		Val O	Val	Gln	Pro	_	Arg 15
15	Ser	Leu	Arg	Leu 20	Ser	Cys	Ala	Ala	Ser 25		Phe	Thr	Phe	_	Ser	Tyr
20	Ala	Met	His 35	Trp	Val	Arg	Gln	Ala 40		Gly	Lys	Gly	Leu .4	_	Trp	Val
25	Ala	Val 50	Ile	Ser	Tyr	Asp	Gly 55		Asn	Lys	Tyr	-	Ala O	Asp	Ser	Val
	Lys 65	Gly	Arg	Phe	Thr	Ile 70	Ser	Arg	Asp	Asn	Ser 75	Lys	Asn	Thr	Leu	Tyr 80
30	Leu	Gln	Met	Asn	Ser 85	Leu	Arg	Ala	Glu	Asp 9		Ala	Val	Tyr	-	Cys 95
35	Ala	Arg	Asp	Arg 100	_	Asp	Trp	Gly	Trp 10		Leu	Phe	Asp	Tyr .11		Gly
	Gln	Gly	Thr 115	Leu	Val	Thr	Val	Ser 120				•				
40	(36)	INFO	ORMA!	rion	FOR	SEQ	ID	NO:3	6							
	(i) \$	SEQUE	NCE (CHARA	ACTER	RISTIC	S:					•				
45		(B) TY	NGTH PE: ai	mino a	cid	acids										
	(ii)	MOLE	CULE .	TYPE:	peptid	le						•				
50	(xi)	SEQU	ENCE	DESC	RIPTI	ON: S	EQ ID	NO:36	3:							
	Gln 1	Val	Gln	Leu	Val 5	Glu	Ser	Gly	Gly	Gly 1		Val	Gln	Pro		Arg .5

	Ser	Leu	Arg	Leu 20	ser	cys	Ala	Ala	Ser 25		Pne	Thr	Pne		Ser 0	Phe.
5	Gly	Met	His 35	Trp	Val'	Arg	Gln	Ala 40		Gly	Lys	Gly	Leu 4		Trp	Val
10	Ala	Tyr 50	Ile	Ser	Ser	Gly	Ser 55		Thr	Ile	Tyr	Tyr 6		Asp	Ser	Val
15	Lys 65	Gly	Arg	Phe	Thr	Ile 70	Ser	Arg	Asp	Asn	Ser 75	Lys	Asn	Thr	Leu	Tyr 80
,,	Leu	Gln	Met	Asn	Ser 85	Leu	Arg	Ala	Glu	Asp 90		Ala	Val	Tyr		Cys 5
20	Ala	Arg		Arg 100	Lys	Gly	Tyr	Ala	Met 105		Tyr	Trp	Gly	Gln 11		Thr
25	Leu	Val	Thr 115	Val	Ser											
	(37) IN	FORMA	NOITA	FOR S	EQ ID	NO:37	7									
	(i)	SEQUE	NCE (CHARA	CTER	ISTIC	S:		٠							
30		(B) T	NGTH PE: ar	nino a	cid	cids										
35	(ii)	MOLE	CULE -	TYPE:	peptid	е		•								
33	(xi)	SEQU	ENCE	DESC	RIPTIO	ON: SE	Q ID I	NO:37:	:							
40	Glu . 1	val	Gln	Leu	Val		Ser	Gly	Gly	Gly 1	Leu .0	Val	Gln	Pro	Gly	Gly 15
	Ser	Leu	_Arq	Leu 20	Ser	Cys	Ala	Ala	Ser 2	Gly 5	Phe	Thr	Phe	Ser	Ser 30	Tyr
45	Tr) Met	Ser 35		Val	Arg	Gln	Ala 4	Pro 0	Gly	Lys	Gly	Leu	. Glu 45	Trp	Val
50	Ala	Asn 50		Lys	Gln	Asp	Gly 5	Ser 5	Glu	Lys	Tyr	Tyr	Val	Asp	Ser	Val
55	Lys 6	s Gly	Arg	Phe	Thr	Ile 70		Arg	Asp	Asn	Ala 75	Lys	. Asn	Ser	Leu	Tyr 80

	Leu	Gln	Met	Asn	Ser 85		Arg	Ala	Glu	Asp 9	Thr 0	Ala	Val	Tyr	Туг	Cys 95
5	Ala	. Arg									•					
10	(38) INF	•														
	(1) S	EQUE	NCE C	нака	CIER	(15)10	5.									
15		(B) TY	NGTH: PE: an	nino ad	cid	acids										
	(ii) N	MOLEC	CULE T	YPE:	peptid	е					•					
20	(xi)	SEQUI	ENCE	DESC	RIPTI	ON: SI	EQ ID	NO:38	В:			-				
	Glu 1		Gln	Leu	Val 5	Glu	Ser	Gly	Gly	Gly 1	_	Val	Gln	Pro	-	Gly L5
25	Ser	Leu	Arg	Leu 20	Ser	Cys	Ala	Ala	Ser 25		Phe	Thr	Phe		Ser O	Phe
30	Gly	Met	His 35	Trp	Val	Arg	Gln	Ala 40		Gly	Lys	Сĵ	Leu 4	_	Trp	Val
	Ala	Tyr 50	Ile	Ser	Ser	Gly	Ser 55		Thr	Ile	Tyr	His 6	_	Asp	Ser	Val
35	Lys 65	Gly	Arg	Phe	Thr	Ile 70	Ser	Arg	Asp	Asn	Ala 75	Lys _.	Asn	Thr	Leu	Phe 80
40	Leu	Gln	Met	Thr	Ser 85	Leu	Arg	Ala	Glu	Asp 90	_	Ala	Met	Tyr		Cys 5
	Ala	Arg.	Met	Arg 100	Lys	Gly	Tyr	Ala	Met 105	Asp 5	Tyr	Trp	Gly	Gln 11	Gly o	Thr
45	Thr	Val	Thr 115	Val	Ser										•	
	(39) INF	ORMA	TION	FOR S	EQ ID	NO:3	9									
50	(i) S	EQUE	NCE C	HARA	CTEF	RISTIC	S: .									
55		(B) TY	NGTH PE: an	nino a	cid	cids										
	(ii) N	MOLEC	HHET	VPE.	nentid	۵.										

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr 5 (40) INFORMATION FOR SEQ ID NO:40 . 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 15 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:40: 20 Lys Thr Ser Leu Arg Pro Gly Lys Gly Ser Ser Asp Tyr Glu Lys Lys 25 (41) INFORMATION FOR SEQ ID NO:41 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 30 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41: Lys Thr Ser Leu Arg Pro Gly Lys Gly Ser Ser Glu Tyr Glu Lys Lys 40 (42) INFORMATION FOR SEQ ID NO:42 (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 50 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:42: Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp His Glu Lys Lys 1 10 15 55

(43) INFORMATION FOR SEQ ID NO:43 (i) SEQUENCE CHARACTERISTICS: 5 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:43: Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Gln Glu Lys Lys (44) INFORMATION FOR SEQ ID NO:44 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:44: 30 Gln Ser Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Gln Glu Lys Lys (45) INFORMATION FOR SEQ ID NO:45 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 40 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:45: Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Pro Glu Lys Lys 50 (46) INFORMATION FOR SEQ ID NO:46 (i) SEQUENCE CHARACTERISTICS: 55 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:46: 5 Gin Thr Ser Lèu Arg Pro Asp Lys Gly Ser Ser Asp Pro Glx Lys Lys (47) INFORMATION FOR SEQ ID NO:47 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 15 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:47: 20 Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Pro Glu Lys Thr (48) INFORMATION FOR SEQ ID NO:48 . 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 30 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:48: 35 Gln Thr Ser Leu Arg Ala Asp Lys Gly Ser Ser Asp Gln Glu Lys Lys 40 (49) INFORMATION FOR SEQ ID NO:49 (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:49: Gln Thr Ser Leu Arg Pro Asp Lys Gly Lys Ser Asp Ser Glu Lys Lys 55

(50) INFORMATION FOR SEQ ID NO:50

(i) SEQUENCE CHARACTERISTICS:

5	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:
	Gln Thr Ser Leu Arg Pro Ala Arg Gly Ser Ser Asp Gln Glu Lys Lys 1 10 15
15	
	(51) INFORMATION FOR SEQ ID NO:51
20	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:
30	Gln Thr Ser Leu Lys Pro Gly Arg Gly Ser Ser Asp Pro Glu Lys Lys 1 5 10 15
35	(52) INFORMATION FOR SEQ ID NO:52
35	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:
	Gin Thr Ser Leu Arg Pro Gly Arg Gly Ser Ser Asp Thr Glu Lys Lys 1 5 10 15
50	(53) INFORMATION FOR SEQ ID NO:53
	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

Gln Ile_Ser_Leu Arg Pro Gly Lys Gly Ser Ser Asp Ser Glu Lys Lys

1 10 15

(54) INFORMATION FOR SEQ ID NO:54

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:
- Gln Thr Ser Leu Arg Pro Gly Lys Gly Asp Ser Asp Glu Asp Lys Lys
 1 5 10 15
 - (55) INFORMATION FOR SEQ ID NO:55
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:
 - Glu Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Ala Asp Lys Lys

 1 10 15
 - (56) INFORMATION FOR SEQ ID NO:56
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:
- Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Glu Asp Lys Lys
 55 1 10 15
 - (57) INFORMATION FOR SEQ ID NO:57

(i) SEQUENCE CHARACTERISTICS:

	· (A) LENGTH: 16 amino acids
	(B) TYPE: amino acid
5	(C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:
10	
	Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Glu Glu Lys Lys 1 10 15
15	
	(58) INFORMATION FOR SEQ ID NO:58
•	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids
-	(B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:
30	Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asx Ala Asx Lys Lys
	1 5 10 15
	(59) INFORMATION FOR SEQ ID NO:59
35	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids
	(B) TYPE: amino acid (C) TOPOLOGY: linear
40	*
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:
45	Wal Mbm Ala Tou Ame Dro Cly Tye Cly Ala Son Aca Cly Aca Aca Cly
	Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Glu Asp Asp Glu 1 5 10 15
50	(60) INFORMATION FOR SEQ ID NO:60
30	(i) SEQUENCE CHARACTERISTICS:
•	(A) LENGTH: 16 amino acids
55	(B) TYPE: amino acid (C) TOPOLOGY: linear
	•
	(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Gln Glu Thr Thr
1 5 10 15

(61) INFORMATION FOR SEQ ID NO:61

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:
- 20 Gln Asn Ser Leu Thr Pro Gly Lys Gly Ser Ser Ser Pro Glu Lys Lys 1 5 10 15
 - (62) INFORMATION FOR SEQ ID NO:62
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:
 - Val Thr Lys Val Arg Pro Gly Lys Gly Asp Ser Asp Lys Lys
 1 10 15
- 40 (63) INFORMATION FOR SEQ ID NO:63
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
- 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:
 - Val Thr Lys Val Arg Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys

 1 10 15
 - (64) INFORMATION FOR SEQ ID NO:64
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

	(B) TYPE: amino acid (C) TOPOLOGY: linear					
5	(ii) MOLECULE TYPE: peptide					
	(xi) SEQUENCE DESCRIPTION: SEQ ID N	10:64:				
10	Val Thr Arg Val Arg Pro Gly I	Lys Gly	Asp Ser 10	Asp i	Ala Glu	Lys Lys 15
	(65) INFORMATION FOR SEQ ID NO:65					
15	(i) SEQUENCE CHARACTERISTICS:					
20	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear			,		
	(ii) MOLECULE TYPE: peptide					
	(xi) SEQUENCE DESCRIPTION: SEQ ID N	NO:65:				
25	Leu Thr Lys Val Arg Pro Gly I	Lys Gly	Asp Ser	Asp S	Ser Glu	Lys Lys 15
30	(66) INFORMATION FOR SEQ ID NO:66					
	(i) SEQUENCE CHARACTERISTICS:					
35	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear		,			
	(ii) MOLECULE TYPE: peptide					
.40	(xi) SEQUENCE DESCRIPTION: SEQ ID N	1O:66:				
45	Val Thr Lys Val Arg Pro Gly I	Lys Gly	Asp Ser	Asp S	Ser Glu	Gln Lys 15
	(67) INFORMATION FOR SEQ ID NO:67					
5Ö	(i) SEQUENCE CHARACTERISTICS:					
	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear					
55	(ii) MOLECULE TYPE: peptide					
	(vi) SEQUENCE DESCRIPTION: SEQ ID N	JO:67·				

Val Thr Lys Val Arg Pro Glu Lys Gly Asp Ser Asp Ala Glu Lys Lys (68) INFORMATION FOR SEQ ID NO:68 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 10 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:68: 15 Val Thr Lys Val Arg Pro Glu Lys Gly Asp Ser Asp Ser Glu Lys Lys 20 (69) INFORMATION FOR SEQ ID NO:69 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:69: 35 Val Thr Lys Val Ser Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 10 (70) INFORMATION FOR SEQ ID NO:70 40 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 45 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:70: 50 Val Arg Ser Gly Lys Gly Glu Ser Asp Ala Glu Lys Lys 55 (71) INFORMATION FOR SEQ ID NO:71 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:
10	Val Thr Ser Val Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
	(72) INFORMATION FOR SEQ ID NO:72
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:
25	Val Ser Ser Val Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
30	(73) INFORMATION FOR SEQ ID NO:73
30	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:
	Val Thr Ser Ala Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 10 15
45	(74) INFORMATION FOR SEQ ID NO:74
	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
55	(ii) MOLECULE TYPE: peptide
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

	Val Ser Ser Ala Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 10 15
5	(75) INFORMATION FOR SEQ ID NO:75
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:
20	Val Thr Ser Ala Arg Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 10 15
	(76) INFORMATION FOR SEQ ID NO:76
25	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:
35	Val Ser Pro Ala Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 10 15
40	(77) INFORMATION FOR SEQ ID NO:77
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:
	Val Thr Lys Ala Arg Pro Gly Lys Gly Asp Ser Asp Val Glu Lys Asn 1 10 15
55	(78) INFORMATION FOR SEQ ID NO:78
	(i) SEQUENCE CHARACTERISTICS:

	(A) LENGTH: 16 amino acids
	(B) TYPE: amino acid (C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:
10	Val Thr Leu Ile Pro Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 10 15
	(79) INFORMATION FOR SEQ ID NO:79
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:
25	Val Thr Leu Leu Gin Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
	(80) INFORMATION FOR SEQ ID NO:80
30	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:
	Val Thr Leu Leu Gln Pro Gly Lys Gly Asp Ser Asp Ala Asp Lys Lys 1 10 15
45	(81) INFORMATION FOR SEQ ID NO:81
	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

	1 5 10 15
5	(82) INFORMATION FOR SEQ ID NO:82
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
4.6	(ii) MOLECULE TYPE: peptide
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:
20	Val Thr Leu Leu Gin Ala Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 10 15
	(83) INFORMATION FOR SEQ ID NO:83
25	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:
35	
	Val Thr Leu Leu Gln Pro Gly Glu Gly Asp Ser Asp Ala Glu Lys Lys 1 10 15
40	(84) INFORMATION FOR SEQ ID NO:84
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:
55	Leu Thr Leu Leu Gln Pro Gly Asn Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
	(85) INFORMATION FOR SEQ ID NO:85

(i) SEQUENCE CHARACTERISTICS:

-	(A) LENGTH: 16 amino acids
	(B) TYPE: amino acid
5	(C) TOPOLOGY: linear
	· ·
	(ii) MOLECULE TYPE: peptide
	(ii) MOLECULE TITE. peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:
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	Wal film You You Cla Dwo Clar You Clar Am Com Am Ala Clar You
	Val Thr Leu Leu Gln Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Ile 1 5 10 15
	. 1 5 10 15
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	(86) INFORMATION FOR SEQ ID NO:86
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	(i) SEQUENCE CHARACTERISTICS:
	(i) SERSENCE CHANACTERISTICS.
20	(A) LENGTH: 16 amino acids
	(B) TYPE: amino acid
	(C) TOPOLOGY: linear
	(=, -= = = = = = = = = = = = = = = = = =
	(ii) MOLECULE TVPS: poplide
	(ii) MOLECULE TYPE: peptide
25	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:
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	Val Thr Leu Phe Gln Pro Gly Gln Gly Asp Ser Asp Pro Glu Lys Lys
30	1 5 10 15
30	
	(87) INFORMATION FOR SEQ ID NO:87
	(i) SEQUENCE CHARACTERISTICS:
35	
	(A) LENGTH: 16 amino acids
	(B) TYPE: amino acid
	(C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide
	· · · · · · · · · · · · · · · · · · ·
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:
	(XI) SEQUENCE DESCRIPTION. SEQ ID NO.67.
45	Val Thr Leu Pro Gln Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
	1 5 10 15
	(88) INCORNATION FOR SEC ID NO.88
	(88) INFORMATION FOR SEQ ID NO:88
50	
	(i) SEQUENCE CHARACTERISTICS:
	·
	(A) LENGTH: 16 amino acids
	(B) TYPE: amino acid
<i>c c</i>	
55	(C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

Val Thr Leu Pro Gln Pro Gly Lys Gly Asp Trp Asp Ala Glu Lys Lys

1 10 15

(89) INFORMATION FOR SEQ ID NO:89

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

Val Thr Phe Leu Ser Pro Gly Gln Gly Asp Ser Asp Ala Glu Lys Lys
1 10 15

- 25 (90) INFORMATION FOR SEQ ID NO:90
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

Glu Ser Ser Ala Arg Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 10 15

- (91) INFORMATION FOR SEQ ID NO:91
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:
- Val Thr Leu Ser Ser Pro Gly Gln Gly Asp Ser Asp Ala Glu Lys Lys

 1 5 10 15

(92) INFORMATION FOR SEQ ID NO:92

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 5 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:92: Val Thr Thr Ala Lys Pro Glu Lys Gly Asp Ser Asp Val Glu Lys Lys 10 15 (93) INFORMATION FOR SEQ ID NO:93 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:93: 30 Val Thr Thr Pro Lys Pro Asp Lys Gly Asp Ser Asp Val Glu Lys Lys 35 (94) INFORMATION FOR SEQ ID NO:94 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 40 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:94: 45 Val Thr Ala Pro Arg Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 50 (95) INFORMATION FOR SEQ ID NO:95 (i) SEQUENCE CHARACTERISTICS: 55 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

٠.	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:
5	Val Thr Ala Pro Lys Pro Gly Lys Gly Thr Ser Ser Ala Glu Lys Lys 1 5 10 15
10	(96) INFORMATION FOR SEQ ID NO:96
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:
25	Val Thr Thr Pro Lys Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 1 5 10 15
	(97) INFORMATION FOR SEQ ID NO:97
30	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear
35	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:
40	Val Ser Ala Pro Lys Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 1 5 10 15
45	(98) INFORMATION FOR SEQ ID NO:98
	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
. 55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

Val Thr Ala Pro Arg Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys (99) INFORMATION FOR SEQ ID NO:99 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:99: Val Thr Ala Pro Lys Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys (100) INFORMATION FOR SEQ ID NO:100 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:100: Val Thr Ala Pro Lys Pro Asp Lys Gly Val Ser Ser Ala Glu Lys Lys (101) INFORMATION FOR SEQ ID NO:101 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:101: Val Thr Ala Pro Lys Ser Glu Lys Gly Val Ser Ser Ala Glu Lys Lys

(i) SEQUENCE CHARACTERISTICS:

(102) INFORMATION FOR SEQ ID NO:102

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	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
5	(ii) _MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:
10	Phe Thr Ala Pro Lys Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 1 5 10 15
	(103) INFORMATION FOR SEQ ID NO:103
15 .	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:
25	Leu Thr Ala Pro Lys Pro Gly Arg Gly Val Ser Ser Ala Glu Lys Lys 1 10 15
30	(104) INFORMATION FOR SEQ ID NO:104
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:
	Val Thr Ala Pro Lys Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Arg 1 5 10 15
45	(105) INFORMATION FOR SEQ ID NO:105
	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
55	(ii) MOLECULE TYPE: peptide
- -	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

Val Ser Ala Pro Lys Pro Gly Lys Glu Gly Ser Ser Ala Glu Lys Lys 1 5 10 15 (106) INFORMATION FOR SEQ ID NO:106

- ·(i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid

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- (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:
- Val Thr Ala Pro Lys Pro Arg Lys Gly Ala Ser Ser Ala Glu Lys Lys

 1 10 15
 - (107) INFORMATION FOR SEQ ID NO:107
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:
 - Val Thr Phe Leu Ser Pro Gly Gln Gly Asn Ser Asp Ala Glu Leu Pro 1 5 10 15
 - (108) INFORMATION FOR SEQ ID NO:108
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:
 - Val Thr Phe Leu Ser Pro Gly Gln Gly Asn Ser Asp Glu Asp Leu Pro
 1 10 15
- 55 (109) INFORMATION FOR SEQ ID NO:109
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear

5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:
10	Val Thr Leu Ser Ser Pro Gln Arg Gly Asp Ser Asp Ala Glu Lys Lys 1 10 15
15	(110) INFORMATION FOR SEQ ID NO:110 (i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:
	Val Thr Ala Pro Lys Ser Ser Lys Gly Gly Ser Ser Ala Glu Lys Lys 1 10 15
30	(111) INFORMATION FOR SEQ ID NO:111
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:
45	Gln Thr Ser Pro Thr Pro Gly Lys Gly Ser Ser Asp Pro Glu Lys Lys 1 5 10 15
	(112) INFORMATION FOR SEQ ID NO:112
50	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
33	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:112:

Gln Ile Ser Leu Ile Pro Gly Lys Gly Ser Tyr Asp Asp Glu Lys Lys 1 5 10 15

5	(113) INFORMATION FOR SEQ ID NO:113
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
15	(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:113:
20	Val Thr_Ala Leu Lys Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 1 10 15
	(114) INFORMATION FOR SEQ ID NO:114
25	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:114:
35	Val Thr Ala Leu Lys Ser Asp Lys Gly Ala Ser Ser Gly Glu Lys Lys 1 10 15
40	(115) INFORMATION FOR SEQ ID NO:115
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
•	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:115:
	Val Thr Pro Pro Ser Pro Gly Gln Gly Asp Ser Ala Ala Glu Lys Lys 1 10 15
55	(116) INFORMATION FOR SEQ ID NO:116
	(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:116: Val Thr Pro Pro Ser Pro Gly Gln Gly Asp Ser Ala Arg Glu Lys Lys 10 (117) INFORMATION FOR SEQ ID NO:117 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH. 16 amino acids (B) TYPE: amino acid 20 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:117: 25 Val Thr Val Arg Lys Pro Gly Lys Gly Asp Ser Ser Asp Glu Lys Lys . 30 (118) INFORMATION FOR SEQ ID NO:118 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 35 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:118: Gln Thr Ser Val Arg Leu Gly Gln Gly Ser Ser Asp Pro Glu Lys Lys 45 (119) INFORMATION FOR SEQ ID NO:119 (i) SEQUENCE CHARACTERISTICS: 50 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 55 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:

Lys Thr Ser Leu Arg Pro Trp Lys Gly Ser Ser Asp Ser Asp Lys Lys 1 5 10 15

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J	(120) INFORMATION FOR SEQ ID NO:120
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
15	(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:
20	Gln Thr Asp Val Thr Gln Gly Gln Gly Ser Ser Gln Pro Glu Lys Lys 1 5 10 15
	(121) INFORMATION FOR SEQ ID NO:121
25	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:
35	Gln Thr Ala Val Ser Gln Gly Gln Gly Ser Ser Gln Ser Glu Lys Lys 1 5 10 15
	(122) INFORMATION FOR SEQ ID NO:122
40	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:
50	Leu Thr Ala Pro Arg Thr Asn Arg Gly Ser Ser Asp Ser Glu Lys Lys 1 10 15
55	(123) INFORMATION FOR SEQ ID NO:123
	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids

	(B) TYPE: amino acid (C) TOPOLOGY: linear
•	(ii) MOLECULE TYPE: peptide
5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:
10	Val Thr Ala Pro Ser Ser His Arg Gly Ser Ser Asp Thr Glu Lys Lys 1 5 10 15
	(124) INFORMATION FOR SEQ ID NO:124
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:124:
25	
	Leu Leu Ser Leu Ser Pro Leu Lys Gly Asp Ser Asp Pro Glu Lys Val 1 5 10 15
30	(125) INFORMATION FOR SEQ ID NO:125
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:125:
	Val Thr Ala Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Lys Leu 1 10 15
45	
	(126) INFORMATION FOR SEQ ID NO:126
50	(i) SEQUENCE CHARACTERISTICS:
-	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
55	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:126:

Val Thr Ile Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Lys Leu
1 10 15

lu Lys Leu 15
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	(ii) MOLECULE TYPE: peptide
5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:
	Ala Val Ser Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Pro Ser 1 5 10 15
10	(131) INFORMATION FOR SEQ ID NO:131
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:
25	Tyr Leu Pro Pro Thr Pro Gly Val Ile Arg Ser Thr Ala Met Lys Leu 1 5 10 15
	(132) INFORMATION FOR SEQ ID NO:132
30	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:
40	Tyr Leu Pro Pro Thr Pro Gly Val Ile Arg Ser Thr Ala Met Arg Leu 1 5 10 15
45	(133) INFORMATION FOR SEQ ID NO:133
45	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:

	Tyr Leu Pro Pro Thr Pro Gly	Leu Ile	Arg Ser 10	Thr Ser	Met Lys Leu 15
5	(134) INFORMATION FOR SEQ ID NO:134				
	(i) SEQUENCE CHARACTERISTICS:				
10	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear				
45	(ii) MOLECULE TYPE: peptide				
	(xi) SEQUENCE DESCRIPTION: SEQ ID	NO:134:			·
20	Tyr Leu Pro Pro Thr Pro Gly	Leu Ile	Arg Ser 10	Thr Ser	Val Lys Leu 15
	(135) INFORMATION FOR SEQ ID NO:135				
25	(i) SEQUENCE CHARACTERISTICS:				
	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear	Y			
30	(ii) MOLECULE TYPE: peptide				
	(xi) SEQUENCE DESCRIPTION: SEQ ID	NO:135:			
35 .	Tyr Leu Pro Pro Thr Pro Gly	Val Ile	Arg Ser 1	Thr Ala (Glu Lys Leu 15
40	(136) INFORMATION FOR SEQ ID NO:136				
40	(i) SEQUENCE CHARACTERISTICS:				
45	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear				
	(ii) MOLECULE TYPE: peptide				
50	(xi) SEQUENCE DESCRIPTION: SEQ ID	NO:136:			
	Tyr Leu Pro Pro Thr Pro Gly V	Val Ile i	Arg Ser T 10	hr Ala G	ly Lys Leu 15
55	(137) INFORMATION FOR SEQ ID NO:137				
	(i) SEQUENCE CHARACTERISTICS:				

(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:137: Tyr Leu Pro Ala Thr Pro Gly Val Val Arg Ser Ser Ala Gly Met Leu 10 (138) INFORMATION FOR SEQ ID NO:138 (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:138: 25 Ser Leu Pro Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Lys Leu (139) INFORMATION FOR SEQ ID NO:139 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 35 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:139: Ser Leu Pro Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Asn Lys Leu 10 45 (140) INFORMATION FOR SEQ ID NO:140 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 50 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

Ser Leu Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Ser Glu Lys Leu
1 10 15

(141) INFORMATION FOR SEQ ID NO:141

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid

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- (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

Ser Leu Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Asp Lys Leu
1 5 10 15

(142) INFORMATION FOR SEQ ID NO:142

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi). SEQUENCE DESCRIPTION: SEQ ID NO:142:

Ser Leu Pro Pro Arg Pro Gly Arg Val Arg Ser Ser Ser Glu Lys Leu
1 10 15

- 40 (143) INFORMATION FOR SEQ ID NO:143
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - ... (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

Ser Leu_Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Ser Glu Gln Leu
1 10 15

(144) INFORMATION FOR SEQ ID NO:144

(i) SEQUENCE CHARACTERISTICS:

	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:144:
10	Ser Leu Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Ser Glu Thr Leu 1 5 10 15
	(145) INFORMATION FOR SEQ ID NO:145
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:145:
25	Ser Leu Pro Pro Lys Pro Gly Lys Ile Arg Ser Ser Thr Gly Lys Leu 1 5 10 15
30	(146) INFORMATION FOR SEQ ID NO:146
	(i) SEQUENCE CHARACTERISTICS:
· 35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:146:
45	Ser Leu Pro Pro Lys Pro Gly Arg Ile Arg Ser Ser Thr Gly Lys Leu 1 5 10 15
45	(147) INFORMATION FOR SEQ ID NO:147
	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
£	(ii) MOLECULE TYPE: peptide
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:147:
	,

Ser Leu Pro Pro Lys Pro Gly Lys Ile Arg Ser Ser Thr Gly Gln Leu (148) INFORMATION FOR SEQ ID NO:148 (i) SEQUENCE CHARACTERISTICS: 10 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:148: Ser Leu Pro Pro Glu Pro Gly Lys Ile Arg Ser Ser Thr Gly Arg Leu 20 (149) INFORMATION FOR SEQ ID NO:149 25 (i) SEQUENCE CHARACTERISTICS: . (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 30 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:149: 35 Ser Leu Ala Pro Ser Pro Gly Lys Ile Arg Ser Thr Ala Glu Lys Leu (150) INFORMATION FOR SEQ ID NO:150 40 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 45 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:150: Ser Leu Pro Pro Arg Pro Gly Lys Ile Arg Ser Ser Thr Gly Asn Val 55 (151) INFORMATION FOR SEQ ID NO:151

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:151: Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Lys Leu 10 (152) INFORMATION FOR SEQ ID NO:152 (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:152: 25 Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Asp Lys Leu (153) INFORMATION FOR SEQ ID NO:153 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 35 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:153: 40 Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Asn Leu (154) INFORMATION FOR SEQ ID NO:154 45 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 50 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:154: 55

Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Ala Val Glu Lys Leu (155) INFORMATION FOR SEQ ID NO:155 (i) SEQUENCE CHARACTERISTICS: 10 (A) LENGTH: 15 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:155: Ser Leu Pro Pro Arg Pro Gly Lys Arg Ser Ser Ala Glu Lys Leu 20 (156) INFORMATION FOR SEQ ID NO:156 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 30 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:156: 35 Ser Leu Ala Pro Ser Pro Gly Lys Val Arg Ser Thr Val Glu Arg Leu (157) INFORMATION FOR SEQ ID NO:157 40 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 45 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:157: 50 Ser Leu Ala Pro Ser Pro Asp Lys Ile Arg Ser Thr Pro Asp Lys Leu

(158) INFORMATION FOR SEQ ID NO:158

(i) SEQUENCE CHARACTERISTICS:

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	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:158:
10	Ser Leu_Ala Leu Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Lys Leu 1 5 10 15
	(159) INFORMATION FOR SEQ ID NO:159
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:159:
25	Ser Leu Pro Leu Ser Ala Gly Lys Val Arg Ser Thr Ala Glu Lys Leu 1 5 10 15
30	(160) INFORMATION FOR SEQ ID NO:160
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:160:
•	Ser Leu Ala Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Tyr Leu 1 5 10 15
45	(161) INFORMATION FOR SEQ ID NO:161
	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
55	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:161:

	Ser Leu Pro Leu Thr Pro Gly Leu Ile Arg Ser Thr Ala Glu Lys Leu 1 5 10 15
5	(162) INFORMATION FOR SEQ ID NO:162
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:162:
20	Ser Leu Pro Leu Thr Pro Arg Val Ile Arg Ser Thr Ala Glu Lys Leu 1 5 10 15
	(163) INFORMATION FOR SEQ ID NO:163 (i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:163:
35	Phe Leu His Pro Thr Pro Gly Thr Asp Ser Ser Ser Thr Glu Lys Leu 1 5 10 15
	(164) INFORMATION FOR SEQ ID NO:164
40	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:164:
50	Phe Leu Leu Pro Thr Pro Gly Thr Asp Ser Ser Ser Thr Glu Arg Leu 1 5 10 15
55	(165) INFORMATION FOR SEQ ID NO:165

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids (B) TYPE: amino acid

	(C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:165:
10	Phe Leu His Pro Thr Arg Val Thr Asp Ser Ser Ser Thr Glu Lys Leu 1 5 10 15
15	(166) INFORMATION FOR SEQ ID NO:166 (i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:166:
	Leu Leu Pro Pro Thr Pro Gly Thr Asn Ser Ser Ser Asn Asp Lys Leu 1 5 10 15
30	(167) INFORMATION FOR SEQ ID NO:167
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:167:
45	Val Leu Pro Leu Ser Pro His Arg Ile Arg Ser Glu Ser Glu Asn Leu 1 5 10 15
	(168) INFORMATION FOR SEQ ID NO:168
50	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
55	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:168:

Ser Leu Ala Pro Ser Pro Ala Lys Phe Arg Ser Thr Ala Glu Arg Asp (169) INFORMATION FOR SEQ ID NO:169 5 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 10 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:169: 15 Arg Ile Arg Ser Asp Pro Glu Lys Lys 20 (170) INFORMATION FOR SEQ ID NO:170 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:170: Val Thr Ala Pro Arg Pro Gly Arg Val Arg Ser Asp Pro Glu Lys Lys 35 (171) INFORMATION FOR SEQ ID NO:171 40 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 45 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:171: 50 Val Thr Gly Pro Arg Pro Gly Arg Ile Arg Ser Asp Pro Glu Lys Lys 55 (172) INFORMATION FOR SEQ ID NO:172

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:172: Val Thr Gly Pro Arg Pro Gly Arg Ile Arg Ser Asp Pro Asp Lys Lys 10 (173) INFORMATION FOR SEQ ID NO:173 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:173: 25 Val Thr Gly Pro Arg Pro Gly Arg Val Arg Ser Asp Pro Glu Lys Lys (174) INFORMATION FOR SEQ ID NO: 174 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 35 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:174: Val Thr Gly Pro Arg Pro Gly Arg Ile Arg Ser Asp Pro Xaa Lys Lys 45 (175) INFORMATION FOR SEQ ID NO:175 (i) SEQUENCE CHARACTERISTICS: 50 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:175: 55

Val Thr Ala Pro Arg Pro Gly Arg Ile Arg Ser Glu Ser Glu Arg Lys
1 10 15

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5	(176) INFORMATION FOR SEQ ID NO:176
	(i) SEQUENCE CHARACTERISTICS:
. 10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:176:
20	Val Thr Gly Pro Ser Arg Gly Arg Ile Arg Ser Asp Pro Glu Lys Lys 1 10 15
20	(177) INFORMATION FOR SEQ ID NO:177
	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:177:
35	Val Thr Val Pro Arg Pro Ser Arg Ile Arg Ser Glu Ser Glu Arg Lys 1 5 10 15
	(178) INFORMATION FOR SEQ ID NO:178
40	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:178:
50 _.	Val Thr Ala Pro Gly Pro Gly Arg Ile Arg Ser Glu Ser Glu Arg Lys 1 5 10 15
55	· (179) INFORMATION FOR SEQ ID NO:179
30	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear

5	(ii) MOLECULE TYPE: peptide
J	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:179:
10	Gln Thr Ser Val Arg Pro Gly Arg Val Arg Ser Asp Pro Glu Arg Lys 1 5 10 15
	(180) INFORMATION FOR SEQ ID NO:180
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:180:
25	Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Glu Arg Lys 1 10 15
	(181) INFORMATION FOR SEQ ID NO:181
30	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
35	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:181:
.40 `	Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Glu Lys Lys 1 5 10 15
45	(182) INFORMATION FOR SEQ ID NO:182
	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:182:
	Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Glu Pro Glu Lys Lys 1 5 10 15

(183) INFORMATION FOR SEQ ID NO:183

(i) SEQUENCE CHARACTERISTICS: 5 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:183: Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Glu Pro Asp Lys Lys 10 15 15 (184) INFORMATION FOR SEQ ID NO:184 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:184: Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ala Glu Pro Glu Lys Lys 1 10 15 30 (185) INFORMATION FOR SEQ ID NO:185 (i) SEQUENCE CHARACTERISTICS: 35 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:185: 45 Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asx Pro Glx Lys Lys 1 10 15 (186) INFORMATION FOR SEQ ID NO:186 50 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 55 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:186:

Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Asx Lys Lys
1 5 10 15

- (187) INFORMATION FOR SEQ ID NO:187

 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (A) ELNOTTI. TO attition
 - (B) TYPE: amino acid (C) TOPOLOGY: linear

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- (0) 101 0100 11 111 1001
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:187:

Gln Thr Ser Val Arg Pro Gly Gln Val Arg Ser Asp Pro Glu Arg Lys
1 5 10 15

- 25 (188) INFORMATION FOR SEQ ID NO:188
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:188:

Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser His Pro Glu Lys Lys
1 10 15

- (189) INFORMATION FOR SEQ ID NO:189
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:189:
- Gln Thr Ser Val Arg Pro Gly Asn Val Arg Ser Asp Pro Asp Lys Lys

 1 5 10 15

(190) INFORMATION FOR SEQ ID NO:190

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:190: Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Glu Lys Thr 10 15 (191) INFORMATION FOR SEQ ID NO:191 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:191: Gln Thr Ser Val Arg Pro Gly Thr Val Arg Ser Glu Pro Glu Lys Lys 30 (192) INFORMATION FOR SEQ ID NO:192 (i) SEQUENCE CHARACTERISTICS: 35 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:192: 45 Gln Thr Ser Val Arg Pro Glu Lys Val Arg Ser Glu Pro Asp Lys Lys 1 (193) INFORMATION FOR SEQ ID NO:193 50 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 55 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:193:-

Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Glu Ser Asp Lys Lys

1 10 15

(194) INFORMATION FOR SEQ ID NO:194

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid

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- (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:194:
- Gln Thr Ser Val Arg Pro Gly Glu Val Arg Ser Glu Pro Asp Lys Lys
 1 5 10 15
 - (195) INFORMATION FOR SEQ ID NO:195
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:195:
 - Gln Thr Ser Val Arg Pro Gly Asx Val Arg Ser Asx Pro Glx Arg Lys

 1 10 15
- 40 (196) INFORMATION FOR SEQ ID NO:196
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:196:
 - Gin Thr Ser Val Ser Pro Gly Lys Val Arg Ser Asp Pro Glu Lys Lys
 1 5 10 15
 - (197) INFORMATION FOR SEQ ID NO:197
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids (B) TYPE: amino acid

	(C) TOPOLOGY: linear							
5	(ii) MOLECULE TYPE: peptide							
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:197	7 :						
10	Gln Thr Ser Val Arg Pro Gly Lys	Val	Asn Ser 10	Asp	Pro	Glu	Lys I	.ys
15	(198) INFORMATION FOR SEQ ID NO:198 (i) SEQUENCE CHARACTERISTICS:					~		
20	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear							
	(ii) MOLECULE TYPE: peptide							
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:198	3:						
	Gln Thr Ser Val Arg Pro Gly Lys 1 5	Val	Arg Ser 10	Asp	Pro	Asp	Thr L	ys _.
30	(199) INFORMATION FOR SEQ ID NO:199			•	•			
	(i) SEQUENCE CHARACTERISTICS:							
35	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear							
	(ii) MOLECULE TYPE: peptide							
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:199):						
45	Gln Thr Ser Val Arg Pro Lys Lys 1	Val	Arg Ser 10	Asp I	Pro C	Slx 1	Lys Ly 15	's
45	(200) INFORMATION FOR SEQ ID NO:200							
	(i) SEQUENCE CHARACTERISTICS:							
50	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear							
55	(ii) MOLECULE TYPE: peptide							
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:200) :						•
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(204) INFORMATION FOR SEQ ID NO:204

(i) SEQUENCE CHARACTERISTICS:

Gln '	Thr Ser	Val 2	Arg Pro 5	Lys	Lys 7	/al	Arg Pho	a Asp	Pro	G1u	Lys L 15
(201) IN	FORMATIC	N FOR	SEQ ID NC):201				-			
(i) S	EQUENCE	CHARA	CTERISTIC	CS:			*******				
	(A) LENGT (B) TYPE: (C) TOPOL	amino ac	id								
(ii) N	MOLECULE	TYPE: p	eptide								
(xi)	SEQUENC	E DESCI	RIPTION: S	SEQ ID	NO:201	:					
Gln 1	Thr Se	r Val	Arg Se 5	r Gly	' Lys	Val	Arg Se	er Glu	Pro	Glu	Thr I
(202) IN	FORMATIC	ON FOR	SEQ ID NO	0:202							
. (i) S	EQUENCE	CHARA	CTERISTI	CS:							
	(A) LENGT (B) TYPE: (C) TOPOI	amino ad	id .								
(ii) !	MOLECULE	E TYPE: ¡	peptide								
(xi)	SEQUENC	E DESCI	RIPTION: S	SEQ ID	NO:202	:-					
Val 1	Thr As	n Leu	Arg Pr	o Gly	Lys	Val	Arg Se 10	r Asp	Ala	Glu	Lys L 15
(203) IN	FORMATIC	ON FOR	SEQ ID NO	0:203							
(i) S	EQUENCE	CHARA	CTERISTI	CS:	•						
	(A) LENGT (B) TYPE: (C) TOPOI	amino ad	id								
	MOLECULE	E TYPE: I	peptide								
(ii) ł											

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:204: Gln Thr Ser Val Ser Pro Gly Asn Ile Arg Ser Glu Ser Asp Lys Lys 10 10 1 (205) INFORMATION FOR SEQ ID NO:205 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:205: 25 Lys Thr Ser Val Thr Pro Gly Lys Phe Arg Ser Glu Pro Glu Lys Lys 30 (206) INFORMATION FOR SEQ ID NO:206 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 35 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:206: Val Thr Leu Leu Pro Pro Gly Arg Val Arg Ser Asp Ala Glu Lys Lys 45 (207) INFORMATION FOR SEQ ID NO:207 50 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 55 · (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:207:

Val Thr Leu Leu Pro Pro Gly Glu Val Arg Ser Asp Ala Glu Lys Lys 1 5 10 15 (208) INFORMATION FOR SEQ ID NO:208

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

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- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:208:

Val Thr Leu Pro Pro Pro Gly Glx Val Arg Ser Asp Ala Glu Arg Lys

1 10 15

(209) INFORMATION FOR SEQ ID NO:209

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:209:
- Val Thr Leu Pro Pro Pro Gly Glx Val Arg Ser Asx Ala Glx Asn Lys

 1 10 15
- (210) INFORMATION FOR SEQ ID NO:210
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:210:

Val Thr Leu Pro Pro Pro Gln Gln Val Arg Ser Asp Ala Glu Lys Lys

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- 55 (211) INFORMATION FOR SEQ ID NO:211
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids (B) TYPE: amino acid

	(C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:211:
10	Val Thr Leu Pro Pro Pro Gly Gln Val Thr Ser Asp Ala Glu Lys Lys 1 10 15
	(212) INFORMATION FOR SEQ ID NO:212
15	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:212:
25	Val Thr Leu Pro Pro Ala Gly Gln Val Arg Ser Asp Ala Glu Lys Arg 1 5 10 15
30	(213) INFORMATION FOR SEQ ID NO:213
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:213:
45	Ala Leu Ser Pro Ser Ser Gly Gln Ser Ser Ser Ala Ser Glu Arg Leu 1 5 10 15
	(214) INFORMATION FOR SEQ ID NO:214
50	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
55	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:214:

	1 5 10 15
5	Ser Arg Gly Asp Ser Gln Arg Pro Glu Ser 20 25
10	(215) INFORMATION FOR SEQ ID NO:215
10	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:215:
	Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Val
25	Ser Arg Gly Asp Ser Gln Arg Pro Glu Ser 20 25
20	(046) INFORMATION FOR SEQ ID NO 316
30	(216) INFORMATION FOR SEQ ID NO:216
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:216:
45	Glu Lys Val Gly Gly Leu Gln Pro Gly Thr Gly Ala Pro Gly Lys Ala 1 5 10 15
	Ser Arg Gly Asp Ser Gln Arg Pro Glu Ser 20 25
50	(217) INFORMATION FOR SEQ ID NO:217
	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:217:

Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala

Ser Lys Gly Asn Ser Gln Arg Ala Glu Ser 20 25

(218) INFORMATION FOR SEQ ID NO:218

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:218:

Glu Lys Met Gly Gly Leu Gin Pro Gly Arg Gly Thr Pro Gly Lys Ala 1 5 10 15

Ser Lys Gly Asn Ser Gln Arg Ala Glu Ser 20 25

(219) INFORMATION FOR SEQ ID NO:219

- (i) SEQUENCE CHARACTERISTICS:
 - .. (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:219:

Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala 1 5 10 15

Ser Lys Gly Thr Ser Gln Arg Ala Glu Ser

(220) INFORMATION FOR SEQ ID NO:220

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:220:
5	Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala 1 5 10 15
10	Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr 20 25
	(221) INFORMATION FOR SEQ ID NO:221
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:221:
25	Glu Lys Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Gly Lys Al 1 5 10 15
30	Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr 20 25
35	(222) INFORMATION FOR SEQ ID NO:222
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
1 5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:222:
	Glu Asn Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala 1 5 15
50	Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr 20 25
	(223) INFORMATION FOR SEQ ID NO:223

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear

_	(ii) MOLECULE TYPE: peptide
5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:223:
10	Glu Lys Val Gly Gly Leu Gln Ser Gly Arg Gly Thr Pro Gly Lys Ala 1 5 10 15
	Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr 20 25
15	(224) INFORMATION FOR SEQ ID NO:224
	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:224:
30	Glu Lys Val Gly Gly Leu Gln Ser Gly Arg Gly Thr Pro Gly Lys Ala 1 5 10 15
	Ser Lys Gly Thr Ser Gln Arg Ala Glu Ser 20 25
35	(225) INFORMATION FOR SEQ ID NO:225
	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:225:
50	Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala 1 5 10 15
	Ser Lys Gly Ile Ser Gln Arg Ala Glu Arg 20 25
55	(226) INFORMATION FOR SEQ ID NO:226
	(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide . (xi) SEQUENCE DESCRIPTION: SEQ ID NO:226: Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ser 10 . 1. . Ala Lys Gly Asx Ser Glx Arg Ala Gln Ser 15 (227) INFORMATION FOR SEQ ID NO:227 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:227: Glu Lys Val Gly Gly Leu Gln Pro Gly Ser Gly Thr Pro Gly Lys Ala 30 10 Ser Lys Gly Asn Ser Gln Arg Ala Glu Ser 20 35 (228) INFORMATION FOR SEQ ID NO:228 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 45 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:228: Glu Lys Val Gly Gly Leu Gln Pro Gly Ser Gly Thr Pro Gly Lys Ala 50 Ser Lys Gly Ser Ser Gln Arg Ala Glu Ser 25 20 55 (229) INFORMATION FOR SEQ ID NO:229

	(i) SEQUENCE CHARACTERISTICS:
5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:229:
	Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Arg Lys A 1 5 10 15
15	Ser Lys Gly Asn Ser Gln Arg Ala Glu Ser 20 25
20	(230) INFORMATION FOR SEQ ID NO:230
	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30 .	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:230:
35	Glu Lys Met Gly Asn Leu Gln Pro Gly Ser Gly Thr Pro Gly Lys Ala 1 5 10 15
	Ser Lys Gly Asn Ser Gln Arg Pro Asp Ser 20 25
40	(231) INFORMATION FOR SEQ ID NO:231
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:231:
55	Glu Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 . 15
-	

Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr 20 25

(232) INFORMATION FOR SEQ ID NO:232

•	(i) SEQUENCE CHARACTERISTICS:
5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:232:
15	Glu Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Ala Pro Glu Lys Asp 1 10 15
	Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr 20 25
20	(233) INFORMATION FOR SEQ ID NO:233
	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids
	(B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:233:
	Glu Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Arg Asp
35	1 5 10 15
	Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr 20 25
40	(234) INFORMATION FOR SEQ ID NO:234
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
-	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:234:

	Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
5	Ser Lys Gly Asn Ala Lys Arg Ser Glu Thr 20 25
10	(235) INFORMATION FOR SEQ ID NO:235 (i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:235:
	Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
25	Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
	(236) INFORMATION FOR SEQ ID NO:236
30	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:236:
	Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Asp Lys Asp 1 10 15
45	Asn Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
	(237) INFORMATION FOR SEQ ID NO:237
50	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:237:
5	Glu Lys Val Gly Gly Leu Thr Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 10 15
	Ser Lys Gly Asn Gly Arg Arg Ser Glu Thr 20 25
10	(238) INFORMATION FOR SEQ ID NO:238
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:238:
25	Glu Met Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
	Ser Lys Gly Asn Asp Arg Arg Ser Glu Thr 20 25
30	(239) INFORMATION FOR SEQ ID NO:239
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:239:
45 .	Glu Met Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys As 1 5 10 15
	Ser Lys Gly Asn Asp Lys Arg Ser Glu Thr 20 25
50	(240) INFORMATION FOR SEQ ID NO:240
	(i) SEQUENCE CHARACTERISTICS:

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(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

	(II) MOLECULE TYPE: pepude
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:240:
5	Glu Met Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
10	Ser Lys Gly Asn Ala Lys Arg Ser Glu Thr 20 25
	(241) INFORMATION FOR SEQ ID NO:241
15	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:241:
25	
	Glu Gln Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
30	Ser Lya Gly Asn Ala Lys Lys Ser Glu Thr 20 25
35	(242) INFORMATION FOR SEQ ID NO:242
	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:242.
	Glu Gln Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
50	Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
55	(243) INFORMATION FOR SEQ ID NO:243
55	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

	(C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:243:
10	Glu Gln Val Gly Gly Leu Lys Pro Gly Lys Gly Ala Pro Glu Lys Asp 1 5 10 15
	Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
15	(244) INFORMATION FOR SEQ ID NO:244
	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
23	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:244:
30	Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asr 1 5 10 15
25	Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
35	(245) INFORMATION FOR SEQ ID NO:245
	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
,,	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:245:
50	Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
	Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
55	(246) INFORMATION FOR SEQ ID NO:246
	(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide . 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:246: Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Glu Lys Asp 10 Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr 15 (247) INFORMATION FOR SEQ ID NO:247 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:247: 30 Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Ser Pro Glu Lys Asp Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr 35 (248) INFORMATION FOR SEQ ID NO:248 (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:248: Asp Lys Met Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp Ser Lys Gly Asn Ala Lys Gln Ser Glu Thr 20 25 55 (249) INFORMATION FOR SEQ ID NO:249

(i) SEQUENCE CHARACTERISTICS:

5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:249:
	Glu Gln Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Asp Lys Asp 1 5 10 15
15	Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
20	(250) INFORMATION FOR SEQ ID NO:250
20	(i) SEQUENCE CHARACTERISTICS:
· 25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:250:
	Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
35	Ser Lys Gly Asn Ala Glu Lys Ser Glu Thr 20 25
40	(251) INFORMATION FOR SEQ ID NO:251
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:251:
	Glu Gln Val Gly Asp Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
55	Thr Lys Gly Asn Ala Arg Arg Ser Glu Thr 20 25

(252) INFORMATION FOR SEQ ID NO:252 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:252: Glu Asn Val Gly Asp Leu Lys Pro Gly Lys Gly Ala Pro Glu Lys Asp Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr 20 (253) INFORMATION FOR SEQ ID NO:253 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:253: Glu Gln Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Ser Asp Lys Asp 10 35 Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr 40 (254) INFORMATION FOR SEQ ID NO:254 (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:254:

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· Glu		n Val	Gly	Gly 5	Leu	Gln	Pro	Gly	Lys Gl 10	y Thr	Pro	Glu	Lys Asp 15
Sei	Lys	s Gly	Asn 20	Ala	Lys	Lys	Ser	Gly 25	Thr				
(255) II	NFORI	MATION	I FOR	SEQ IC) NO:2	55							
· (i)	SEQU	ENCE (CHARA	CTER	ISTICS) ;							
	(B) T	ENGTH YPE: ar	mino ad	cid	ids								
(ii)	MOLE	CULE .	TYPE:	peptide	•								
(xi) SEQI	JENCE	DESC	RIPTIC	N: SE	QIDN	10:255	:					
Asp 1	Glr	yal	Gly	Gly . 5	Leu	Gln	Pro (Gly :	Lys Gly 10	y Thr	Pro	Glu	Lys Asp 15
Thr	. Lys	; Gly	Asn 20	Pro	Lys	Arg	Ser	Glu 25	Thr				
(256) I	NFOR	MATION	FOR	SEQ IC	NO:2	56							
(i)	SEQU	ENCE (CHARA	CTER	ISTICS	3 :				٠			
	(B) T	ENGTH YPE: ar	mino ad	cid	cids								-
(ii)	MOLE	CULE	TYPE:	peptide	•								
(xi) SEQI	JENCE	DESC	RIPTIC	N: SE	Q ID N	IO:256	:					
Asp 1		Val	Gly	Gly 5	Leu (Gln 1	Pro (Sly (Thr	Pro (3lu 1	Lys Asn 15
Thr	Lys	Gly	Asn 20	Pro	Lys	Arg	Ser	Asp 25	Thr				
(257) I	NFOR	MATION	FOR	SEQ IC) NO:2	57							
(i)	SEQU	ENCE (CHARA	CTER	ISTICS	: :							
	(B) T	ENGTH YPE: ar	nino ad	cid	cids								
(ii)	MOLE	CULE	TYPE: (peptide	•								

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:257:

Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Ser Glu Lys Asp
1 5 10 15

Ile Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25

(258) INFORMATION FOR SEQ ID NO:258

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:258:

Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Arg Thr Pro Glu Lys Asp

Asn Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25

(259) INFORMATION FOR SEQ ID NO:259

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:259:

Asp Lys Val Gly Gly Leu Lys Leu Gly Lys Gly Thr Pro Glu Lys Asp

Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25

(260) INFORMATION FOR SEQ ID NO:260

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:260: 5 Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp Ser Lys Gly Asn Ala Asn Thr Ser Glu Thr 10 (261) INFORMATION FOR SEQ ID NO:261 · (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:261: 25 Glu His Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp Ser Lys Gly Asn Ala Gly Arg Ser Glu Thr 30 20 (262) INFORMATION FOR SEQ ID NO:262 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:262: 45 Glu Gln Val Gly Gly Leu Gln Pro Gly Asn Gly Thr Pro Glu Lys Asp Thr Thr Gly Asn Ala Lys Arg Ser Glu Thr 50 20 (263) INFORMATION FOR SEQ ID NO:263 (i) SEQUENCE CHARACTERISTICS: 55

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:263: 5 Glu Lys Glu Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Glu 10 Ser Lys Gly Asp Ser Lys Arg Ala Glu Thr (264) INFORMATION FOR SEQ ID NO:264 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid 20 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:264: Glu Lys Glu Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Glu 1 10 15 30 Ser Lys Gly Asp Ser Lys Arg Pro Glu Thr 35 (265) INFORMATION FOR SEQ ID NO:265 (i) SEQUENCE CHARACTERISTICS: - (A) LENGTH: 26 amino acids (B) TYPE: amino acid 40 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:265: 45 Glu Lys Glu Gly Gly Leu Gln Pro Gly Lys Gly Ser Pro Glu Lys Glu 1 10 15 50 Ser Lys Gly Asp Ser Lys Arg Ala Glu Thr 55 (266) INFORMATION FOR SEQ ID NO:266

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:266: 10 Glu Lys Asp Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp Ser Lys Gly Asp Ser Lys Arg Val Glu Met 15 (267) INFORMATION FOR SEQ ID NO:267 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:267: Glu Gln Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Glu Lys Asp 30 Thr Gly Asp Ala Gln Arg Ser Glu Thr 35 (268) INFORMATION FOR SEQ ID NO:268 (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 45 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:268: 50 Glu Gln Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Glu Lys Asp Thr Thr Gly Asn Ala Lys Gly Ser Glu Thr 20 25 55 (269) INFORMATION FOR SEQ ID NO:269

(i) SEQUENCE CHARACTERISTICS:

	·						
5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear						
	(ii) MOLECULE TYPE: peptide						
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:269:						
	Glu Lys Val Gly Gly Ser Lys Pro Gly Lys Gly Thr Pro Glu Lys As						
15	Ser Lys Gly Asn Ala Lys Thr Ser Glu Thr						
	(270) INFORMATION FOR SEQ ID NO:270						
20	(i) SEQUENCE CHARACTERISTICS:						
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear						
	(ii) MOLECULE TYPE: peptide						
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:270:						
	Ser Asp Gln Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15						
35	Thr Lys Gly Asn Ala Arg Arg Ser Glu Ser 20 25						
	(271) INFORMATION FOR SEQ ID NO:271						
40	(i) SEQUENCE CHARACTERISTICS:						
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear						
	(ii) MOLECULE TYPE: peptide						
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:271:						
	Glu Lys Ile Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Pro 1 5 10 15						
55	Ser Lys Asp Asn Ala Lys Arg Ser Glu Thr 20 25						

(272) INFORMATION FOR SEQ ID NO:272

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	(i) SEQUENCE CHARACTERISTICS:								
5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear								
	(ii) MOLECULE TYPE: peptide								
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:272:								
15	Glu Lys Leu Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Pro 1 5 10 15								
	Ser Lys Asp Asn Ala Lys Arg Ser Glu Thr 20 25								
20	(273) INFORMATION FOR SEQ ID NO:273								
	(i) SEQUENCE CHARACTERISTICS:								
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear								
:	(ii) MOLECULE TYPE: peptide								
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:273:								
35	Glu Lys Leu Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Pro 1 5 10 15								
-	Phe Lys Asp Asn Ala Lys Arg Ser Glu Thr 20 25								
40	(274) INFORMATION FOR SEQ ID NO:274								
	(i) SEQUENCE CHARACTERISTICS:								
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear								
50	(ii) MOLECULE TYPE: peptide								
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:274:								
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1 5 10 15
Met Lys Glu Asn Ala Lys Arg Ser Glu Thr 20 25
(275) INFORMATION FOR SEQ ID NO:275
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:275:
Glu Asn Leu Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Leu
1 5 10 15
Lys Xaa Glu Asn Ala Lys Arg Pro Glu Thr 20 25
(276) INFORMATION FOR SEQ ID NO:276
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:276:
Glu Lys Leu Gly Gly Leu Gln Pro Gly Asn Gly Asp Leu Gly Lys Pro 1 5 10 15
Ser Lys Asp Asn Ala Lys Arg Ser Glu Thr 20 25
(277) INFORMATION FOR SEQ ID NO:277
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 amino acids
(B) TYPE: amino acid (C) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE	DESCRIPTION: SEQ ID NO:277:

Glu Lys Leu Gly Pro Leu Gln Leu Gly Lys Gly Asp Pro Gly Lys Pro 1 10 15

Ser Lys Asp Asp Ala Lys Arg Ser Glu Thr 20 25

(278) INFORMATION FOR SEQ ID NO:278

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:278:
- Glu Gln Leu Gly Gly Leu Gln Pro Gly Gly Gly Thr Pro Gly Lys Pro
 1 10 15

Ser Lys Asp Asn Asp Lys Arg Ser Glu Thr 20 25

(279) INFORMATION FOR SEQ ID NO:279

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:279:

Glu Gln Leu Gly Gly Leu Gln Pro Gly Gly Gly Thr Pro Gly Lys Ala 1 5 10 15

Ser Lys Asp Asn Asp Lys Arg Ser Glu Thr

(280) INFORMATION FOR SEQ ID NO:280

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:280: 5 Glu Gln Val Gly Gly Leu Lys Ala Arg Lys Gly Thr Pro Glu Lys Asp Thr Thr Gly Asn Ala Lys Arg Ser Glu Thr 10 (281) INFORMATION FOR SEQ ID NO:281 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:281: 25 Glu Met Val Gly Val Leu Glu Pro Gly Lys Gly Thr Pro Glu Lys Arg Gln Glu Gly Asn Ala Lys Arg Ser Glu Thr 30 (282) INFORMATION FOR SEQ ID NO:282 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:282: 45 Glu Gln Val Gly Gly Leu Gln Pro Lys Lys Gly Ser Pro Gly Lys Asp 1 Ser Lys Asp Asp Ser Gln Lys Thr Glu Thr 50 20 25 (283) INFORMATION FOR SEQ ID NO:283 55 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:283: 5 Glu Gln Val Gly Gly Leu Gln Pro Lys Lys Gly Ser Pro Gly Lys Asp 10 Ser Lys Asp Asp Ser Gln Lys Thr Glu Arg 15 (284) INFORMATION FOR SEQ ID NO:284 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid 20 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:284: 25 Gln Gln Val Pro Glu Leu Lys Pro Gly Arg Gly Thr Pro Gly Lys Glu 30 Asp Lys Gly Thr Ser Ala Arg Asn Asp Thr (285) INFORMATION FOR SEQ ID NO:285 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:285: 45 Gln Gln Val Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Lys Asp 1 50 Asp Lys Gly Thr Ser Ala Lys Asn Glu Thr 20

(286) INFORMATION FOR SEQ ID NO:286

(i) SEQUENCE CHARACTERISTICS:

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(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:286: Gln Gln Val Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Lys Asp 10 Asp Lys Gly Thr Ser Ala Lys Asn Glu Met 20 15 (287) INFORMATION FOR SEQ ID NO:287 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:287: Gln Gln Lys Pro Glu Leu Lys Pro Gly Lys Gly Ser Pro Gly Gln Glu . 10 Lys Lys Gly Thr Ser Ser Thr Ser Glu Thr 20 35 (288) INFORMATION FOR SEQ ID NO:288 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:288: 50 Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 55 (289) INFORMATION FOR SEQ ID NO:289

	(i) SEQUENCE CHARACTERISTICS:	
5	(A) LENGTH: 26 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear	·
	(ii) MOLECULE TYPE: peptide	
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:289:	
	Glu Gln Gln Pro Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly 1 5 10	Gln Glu 15
15	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25	-
	(290) INFORMATION FOR SEQ ID NO:290	
20	(i) SEQUENCE CHARACTERISTICS:	
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:290:	
	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly 1 5 10	Gln Glu 15
35	Lys Lys Gly Lys Ser Ser Ala Ser Glu Ser 20 25	
40	(291) INFORMATION FOR SEQ ID NO:291	
	(i) SEQUENCE CHARACTERISTICS:	
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:291:	
55	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly 1	Lys Gln 15
	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25	

(292) INFORMATION FOR SEQ ID NO:292

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(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 5 (B) TYPE: amino acid (C) TOPOLOGY: linear 10 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:292: 15 Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 20 (293) INFORMATION FOR SEQ ID NO:293 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids . (B) TYPE: amino acid (C) TOPOLOGY: linear 30 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:293: 35 Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Ser His Gly Lys Gln 1 Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 40 (294) INFORMATION FOR SEQ ID NO:294 45 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 50 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:294:

	1 5 10 15
5	Lys Lys Gly Lys Ser Ser Ala Ser Glu Ser 20 25
10	(295) INFORMATION FOR SEQ ID NO:295
U	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:295:
	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln 1 10 15
? 5	Lys Lys Gly Lys Ser Ser Thr Phe Glu Ser 20 25
30	(296) INFORMATION FOR SEQ ID NO:296 (i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
ŧ0	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:296:
	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln 1 5 10 15
15	Lys Gln Gly Lys Ser Ser Thr Phe Glu Ser 20 25
50	(297) INFORMATION FOR SEQ ID NO:297
5 U	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

'(xi) SEQUENCE DESCRIPTION: SEQ ID NO:297:

Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Glu
1 5 10 15

Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser 20 25

(298) INFORMATION FOR SEQ ID NO:298

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:298:

Glu Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Ser His Gly Lys Gln
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25

(299) INFORMATION FOR SEQ ID NO:299

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:299:

Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln
1 5 10 15

Lys Lys Ser Asn Ser Ser Thr Ser Glu Ser 20 25

(300) INFORMATION FOR SEQ ID NO:300

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:300:
5	Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Ala Pro Gly Gln Glu 1 5 10 15
10	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25
	(301) INFORMATION FOR SEQ ID NO:301
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:301:
25	Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Ala Pro Gly Gln Glu 1 5 10 15
30	Lys Lys Gly Lys Ser Ser Thr Ser Asp Ser 20 25
	(302) INFORMATION FOR SEQ ID NO:302
35	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	· (ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:302:
45	Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Val Pro Gly Gln Gli 1 5 10 15
50	Lys Lys Gly Lys Ser Ser Thr Ser Asp Ser 20 25
	(303) INFORMATION FOR SEQ ID NO:303
55	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:303: 5 Gln Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Ala Pro Gly Lys Gly 10 Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser (304) INFORMATION FOR SEQ ID NO:304 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid 20 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:304: 25 Gln Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Ala Pro Gly Lys Gly (305) INFORMATION FOR SEQ ID NO:305 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 40 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:305: 45 Glu Gln Gln Pro Glu Ala Lys Pro Gly Lys Gly Thr His Gly Lys Gln. 1 10 15 50 Lys Lys Gly Lys Ser Ser Thr Ser Asp Ser 20 25 55 (306) INFORMATION FOR SEQ ID NO:306

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B).TYPE: amino acid

	(C) TOPOLOGY: linear	
5	(ii) MOLECULE TYPE: peptide	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:306:	
10	Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Glu 1 5 10 15	ı
15	Lys Lys Asp Lys Ser Ser Thr Ser Asp Ser 20 25	
	(307) INFORMATION FOR SEQ ID NO;307	
20	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
25	(ii) MOLECULE TYPE: peptide	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:307:	
30	Gin Gin Gin Ala Glu Leu Arg Pro Gly Lys Gly Ala Pro Gly Gin Gly	
30	1 5 10 15	
35		
	1 5 10 15 Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser	•
	1 5 10 15 Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25	
35	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 (308) INFORMATION FOR SEQ ID NO:308	•
35	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser (308) INFORMATION FOR SEQ ID NO:308 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid	
35 40	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser (308) INFORMATION FOR SEQ ID NO:308 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	•
35 40	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser (308) INFORMATION FOR SEQ ID NO:308 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide	ŀ
35 40	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser (308) INFORMATION FOR SEQ ID NO:308 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:308: Gln Gln Gln Ala Glu Leu Lys Pro Gly Arg Gly Thr Pro Gly Gln Glu	

(i) SEQUENCE CHARACTERISTICS:

5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
J	(ii) MOLECULE TYPE: peptide	
	(ii) Moccoocc 111 E. popula	
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:309:	
	Glu Gln Gln Ala Glu Leu Arg Ala Gly Lys Gly Thr P	ro Gly Gln Glu 15
15	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25	
20	(310) INFORMATION FOR SEQ ID NO:310	
20	(i) SEQUENCE CHARACTERISTICS:	
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
30	(xi) SEQUENCE, DESCRIPTION: SEQ ID NO:310:	
• .•	Clare	na clu cla clu
-	Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pr 1 5 10	15
35	Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser 20 25	
	(311) INFORMATION FOR SEQ ID NO:311	
40	(i) SEQUENCE CHARACTERISTICS:	
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:311:	
	Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr 1	Pro Gly His Glu 15
55	Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser	

(312) INFORMATION FOR SEQ ID NO:312 (i) SEQUENCE CHARACTERISTICS: 5 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:312: Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly His Glu 15 Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser 20 20 (313) INFORMATION FOR SEQ ID NO:313 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:313: Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly His Glu 35 Asn Lys Gly Thr Ser Ser Thr Ser Glu Ser 20 40 (314) INFORMATION FOR SEQ ID NO:314 (i) SEQUENCE CHARACTERISTICS:

- - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:314:

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	Gln 1	Gln	Gln	Ala	Glu 5	Val	Arg	Pro	Gly	Lys Gly 10	Thr	Pro Gly	His Glu 15	1
5	Lys	Lys	Gly	Thr 20	Ser	Ser	Thr	Ser	Glu 25					
10	(315) IN	NFORM	MOITAN	N FOR	SEQ II	ONO:	315							
	(i) s	SEQUE	ENCE (CHARA	ACTER	ISTIC	S:							
15		(B) T	ENGTH YPE: a OPOLO	mino a	cid	cids								
	(ii)	MOLE	CULE	TYPE:	peptid	е								
20	(xi)	SEQL	JENCE	DESC	RIPTIO	ON: SE	Q ID N	10:315	:					
25	Gln 1	Gln	Gln	Ala	Glu 5	Leu	Lys	Pro (Gly :	Lys Gly 10	Thr	Pro`Gly	His Glu 15	
	Asn	Lys	Gly	Thr 20	Ser	Ser	Thr	Ser	Glu [*] 25	Ser				
30	(31 <u>6</u>) IN	NFORM	OITAN	N FOR	SEQ II	D NO:	316						·	
	(i) \$	SEQUI	ENĊE (CHARA	ACTER	ISTIC	S:							
35	-	(B) T	ENGTH YPE: a OPOLO	mino a	cid	cids								
	(ii)	MOLE	CULE	TYPE:	peptid	е								
40	(xi)	SEQL	JENCE	DESC	RIPTIO	ON: SE	Q ID N	IO:316	:					
45	Gln (Gln	Gln .	Ala (Glu 1 5	Leu i	Arg I	Pro G	ly I	ys Gly 10	Thr I	Pro Gly	Gln Gln 15	
	Lys :	Lys	Gly	Lys 20	Ser	Ser	Ala	Ser	Glu 25	Ser				
50	(317) IN	NFORM	MATION	N FOR	SEQ II	D NO:	317				•			
	(i) \$	SEQUI	ENCE (CHARA	ACTER	ISTIC	S:							
55	•	(B) T	ENGTH YPE: a OPOLO	mino a	cid	cids								
	(ii)	MOLE	CULE	TYPE:	peptid	е								

His Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:317:

(318) INFORMATION FOR SEQ ID NO:318

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:318:

Glu Gln Gln Val Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu
25 1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser

(319) INFORMATION FOR SEQ ID NO:319

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:319:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15

Lys Gln Gly Thr Ser Ser Thr Ser Glu Ser 20 25

(320) INFORMATION FOR SEQ ID NO:320

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

	(ii) MOLECULE TYPE: peptide			
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:320:			
5			*	
•	Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Th	ur Pro	Gly H	lis Asp 15
10	Asn Lys Gly Thr Ser Ser Thr Ser Glu Ser 20 25			
	(321) INFORMATION FOR SEQ ID NO:321			٠
15	(i) SEQUENCE CHARACTERISTICS:			
	(A) LENGTH: 26 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear			
	(ii) MOLECULE TYPE: peptide			
?5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:321:		•	
	Gln Gln Gln Ala Glu Val Arg Pro Gly Lys Gly Th	r Pro	Gly H	is Glu 15
30	Lys Lys Gly Arg Ser Ser Thr Ser Glu Ser 20 25		·	
35	(322) INFORMATION FOR SEQ ID NO:322			
,,	(i) SEQUENCE CHARACTERISTICS:			
-	(A) LENGTH: 26 amino acids (B) TYPE: amino acid			
10 .	(C) TOPOLOGY: linear			
	(ii) MOLECULE TYPE: peptide			
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:322:			
	Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr 1 5 10	Pro G	ly Gl	n Gln. 15
50	Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser 20 25			
	(323) INFORMATION FOR SEQ ID NO:323	• • •	•	
55	(i) SEQUENCE CHARACTERISTICS:			

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:323: Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln 10 Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser 15 (324) INFORMATION FOR SEQ ID NO:324 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:324: Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln 30 Lys Lys Asp Lys Ser Ser Thr Ser Asp Ser 35 (325) INFORMATION FOR SEQ ID NO:325 (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:325: 50 Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Ser Pro Gly Gln Gln 1 Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser 25 20 55 (326) INFORMATION FOR SEQ ID NO:326

(i) SEQUENCE CHARACTERISTICS:

5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:326:
	Gln His Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln 1 5 10 15
	Lys Lys Asn Lys Ser Ser Thr Ser Glu Ser 20 25
20	(327) INFORMATION FOR SEQ ID NO:327
	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:327:
35	Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln 1 5 10 15
	Asn Lys Asp Lys Ser Ser Thr Ser Glu Ser 20 25
40	(328) INFORMATION FOR SEQ ID NO:328
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:328:
55	Glu Gln Gln Ala Glu Leu Arg Ala Gly Lys Gly Ile Pro Gly Gln Glu 1 5 10 15
	Lys Lya Gly Lys Ser Ser Thr Ser Glu Ser

(329) INFORMATION FOR SEQ ID NO:329 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 5 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:329: Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu 15 Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser-20 20 (330) INFORMATION FOR SEQ ID NO:330 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:330: 35 Gln Gln Gln Ser Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser 40 (331) INFORMATION FOR SEQ ID NO:331 (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:331:

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Gln Gln Gln Thr Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15

5	Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser 20 25
10	(332) INFORMATION FOR SEQ ID NO:332
10	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:332:
25	Glu Gln Gln Ala Glu Leu Arg Thr Gly Lys Gly Thr Pro Gly Gln Glu 1 5 10 15
	Arg Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25
30	(333) INFORMATION FOR SEQ ID NO:333
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:333:
45	Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln 1 5 10 15
	Lys Lys Asp Lys Ser Ser Thr Phe Glu Ser 20 25
50	(334) INFORMATION FOR SEQ ID NO:334
	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:334:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Thr Gly Ala Pro Gly Gln Glu
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25

(335) INFORMATION FOR SEQ ID NO:335

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:335:

Gln Gln Gln Pro Glu Val Arg Pro Gly Lys Gly Thr His Ala Lys Gln
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25

(336) INFORMATION FOR SEQ ID NO:336

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:336:

Gin Gin Gin Pro Glu Val Arg Pro Gly Lys Asp Thr His Ala Lys Gin
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser

(337) INFORMATION FOR SEQ ID NO:337

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:337: 5 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Glu Gln Glu Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 10 (338) INFORMATION FOR SEQ ID NO:338 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:338: 25 Glu Gln Gln Thr Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu Lys Lys Gly Arg Ser Ser Thr Ser Glu Ala 30 20 25 (339) INFORMATION FOR SEQ ID NO:339 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:339: 45 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu 1 Lys Lys Ser Lys Pro Ser Thr Ser Glu Ser 50 20 (340) INFORMATION FOR SEQ ID NO:340

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:340: 5 Gln Gln Gln Ser Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu 10 Lys Lys Ser Lys Pro Ser Thr Ser Glu Ser (341) INFORMATION FOR SEQ ID NO:341 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 20 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:341: 25 Gln Gln Arg Ala Glu Leu Lys Pro Gly Lys Asp Thr Pro Gly Arg Glu 10 30 Lys Lys Asn Lys Pro Ser Thr Ser Glu Ser 20 (342) INFORMATION FOR SEQ ID NO:342 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 40 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:342: 45 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu 1 5 50 Lys Lys Ser Thr Ser Ser Thr Ser Glu Ser 55 . (343) INFORMATION FOR SEQ ID NO:343

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

	(C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:343:
	Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu 1 5 10 15
15	Lys Lys Ser Thr Ser Ser Thr Ser Asp Ser 20 25
	(344) INFORMATION FOR SEQ ID NO:344
20	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:344:
30	Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Ile Gln Gln 1 5 10 15
35	Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser 20 25
	(345) INFORMATION FOR SEQ ID NO:345
40	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:345:
50	Gln Gln Gln Ala Glu Phe Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu 1 5 10 15
55	His Arg Ser Lys Pro Ser Thr Ser Glu Ser 20 25
	(346) INFORMATION FOR SEQ ID NO:346

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 MOLECULAR IMMUNOLOGY vol. 28, no. 4/5, 1991, GB pages 489 - 498 PADLAN A E 'POSSIBLE PROCEDURE FOR REDUCING THE IMMUNOGENICITY OF ANTIBODY VARIABLE DOMAINS WHILE PRESERVING THEIR LIGAND-BINDING PROPERTIES'

P 0 592 106 B1

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Description

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FIELD OF THE INVENTION

[0001] The present invention relates to the development of prediction rules that can be used to accurately model the variable regions (V-regions) of antibodies. The development of these rules and their application in the predictive molecular restructuring of the surfaces of variable domains of non-human monoclonal antibodies enables changing of the surface, i.e., resurfacing, of these monoclonal antibody V-regions to replicate the surface characteristics found on human antibody V-regions. This method of resurfacing non-human monoclonal antibody V-regions to resemble human antibody V-regions is expected to permit the production of functional altered antibodies, which retain the binding parameters of the original non-human monoclonal antibody, with improved therapeutic efficacy in patients due to the presentation of a human surface on the V-region.

BACKGROUND OF THE INVENTION

General Background of Antibodies

[0002] Munne monoclonal antibodies are widely used as diagnostic and therapeutic agents in the treatment of human disease. Mice can be readily immunized with foreign antigens to produce a broad spectrum of high affinity antibodies. Invariably, the introduction of murine or other rodent antibodies into humans results in the production of a human antimouse antibody (HAMA) response due to the presentation of a foreign protein in the body. The production of HAMA in patients can result from the introduction of foreign antibody in a single dose or from extended use in therapy, for example, for the treatment of cancer. Extended use of murine antibody is generally limited to a term of days or weeks in patients before concerns of anaphylaxis arise. Moreover, once HAMA has developed in a patient, future use of murine antibodies for diagnostic or therapeutic purposes is often precluded for the same reasons.

[0003] Beyond ethical considerations, attempts to produce human monoclonal antibodies have not been highly successful for a number of reasons. The production *in vitro* of human monoclonals rarely results in high affinity antibodies. *In vitro* cultures of human lymphocytes yield a restricted range of antibody responses relative to the broad spectrum of reactive antibodies produced *in vivo* through direct immunization of mice. Additionally, in humans, immune tolerance prevents the successful generation of antibodies to self-antigens. All of these factors have contributed to the search for ways to modify the structures of murine monoclonal antibodies to improve their use in patients. Many investigators have attempted to alter, reshape or humanize murine monoclonal antibodies in an effort to improve the therapeutic application of these molecules in patients.

35 Strategies of Antibody Humanization

[0004] The earliest reports of the controlled rearrangement of antibody domains to create novel proteins was demonstrated using rabbit and human antibodies as described by Bobrzecka, K. et al. (Bobrzecka, K., Konieczny, L., Laidler, P. and Rybarska, J. (1980), Immunology Letters 2, pp. 151-155) and by Konieczny et al. (Konieczny, L., Bobrzecka, K., Laidler, P. and Rybarska, J. (1981), Haematologia 14 (I), pp. 95-99). In those reports, the protein subunits of antibodies, rabbit Fab fragments and human Fc fragments, were joined through protein disulfide bonds to form new, artificial protein molecules or chimeric antibodies.

[0005] Recombinant DNA technology was used to construct gene fusions between DNA sequences encoding mouse antibody variable light and heavy chain domains and human antibody light chain (LC) and heavy chain (HC) constant domains to permit expression of the first recombinant "near-human" antibody (chimenc antibody) product (Morrison, S.L., Johnson, M.J., Herzenberg, L.A. and Oi, V.T. (1984), Proc. Natl. Acad. Sci. U.S.A. 81, pp. 6851-6855).

[0006] The kinetics and immune response in man to chimeric antibodies has been examined (LoBuglio, A.F., Wheeler, R.H., Trang, J., Haynes, A., Rogers, K., Harvey, E.B., Sun, L., Ghrayeb, J. and Khazaeli, M.B. (1989), Proc. Natl. Acad. Sci. 86, pp. 4220-4224).

[0007] Chimeric antibodies contain a large number of non-human amino acid sequences and are immunogenic in man. The result is the production of human anti-chimera antibodies (HACA) in patients. HACA is directed against the murine V-region and can also be directed against the novel V-region/C-region (constant region) junctions present in recombinant chimeric antibodies.

[0008] To overcome some of the limitations presented by the immunogenicity of chimeric antibodies, the DNA sequences encoding the antigen binding portions or complementarity determining regions (CDR's) of murine monoclonal antibodies have been grafted by molecular means in the DNA sequences encoding the frameworks of human antibody heavy and light chains (Jones, P.T., Dear, P.H., Foote, J., Neuberger, M.S. and Winter, G. (1986), Nature 321, pp. 522-525; Riechmann, L., Clark, M., Waldmann, H. and Winter, G. (1988), Nature 332, pp. 323-327). The expressed

recombinant products called reshaped or humanized antibodies are comprised of the framework of a human antibody light or heavy chain and the antigen recognition portions, CDR's, of a murine monoclonal antibody. Several patent applications have been filed in this area including, for example, European Patent Application, Publication No. 0239400; European Patent Application, Publication Nos. 0438310A1 and 0438310A2; International Patent Publication No. WO 91/09967; and International Patent Publication No. WO 90/07861.

[0009] However, it is questionable whether European Patent Application (EP), Publication No. 0239400 is truly enabling. It is not assured in this patent that the best fit is made to assure proper presentation of the CDR loops at the antibody combining site.

[0010] EP Publication Nos. 0438310A1 and 0438310A2 go a step beyond EP Publication No. 0239400 by protecting the importance of uniquely selected human frameworks for the human light chain (LC) and heavy chain (HC) V-regions. These V-region frameworks should show a high degree of sequence similarity with the frameworks of the murine monoclonal antibody and present the CDR's in the appropriate configuration. However, the criteria for sequence matching are no more sophisticated than simple homology searching of the antibody protein or DNA databases.

[0011] International Patent Publication No. WO 91/09967 attempts a further variation of the method disclosed in EP Publication No. 0239400. In International Patent Publication No. WO 91/09967, homology of the donor sequences and the acceptor framework is not important, rather it discloses that a selected set of residues in the LC and HC are critically important to humanization. The ability to make changes at these positions is the basis of International Patent Publication No. WO 91/09967.

[0012] International Patent Publication No. WO 90/07861 proposes four important criteria for designing humanized antibodies. 1) Homology between human acceptor and non-human donor sequences. 2) Use donor rather than acceptor amino acids where the acceptor amino acid is unusual at that position. 3) Use donor framework amino acids at positions adjacent to the CDR. 4) Use donor amino acids at framework positions where the sidechain atom is within 3 x 10⁻¹⁰ (3 Angstroms) of the CDR in a 3-D model. The first antibody humanized by this method retained less than 1/3 the affinity of the original monoclonal antibody.

[0013] None of the above methods for designing a humanized antibody are predictable due to the questions that surround CDR framework interactions. By replacement of murine framework with human framework, there is no guarantee of identical conformations for CDR's because i) the V_L-V_H interaction is not identical in all V-regions and ii) accurate prediction of the CDR-framework interactions are key to faithful reproduction of the antigen binding contacts. [0014] The above methods do not offer a general solution to solving the issues surrounding antibody humanization, rather the methods as outlined in each reference above involve a substantial amount of trial and error searching to obtain the desired affinity in the final humanized product. More importantly, there is no guarantee that corrective changes in framework amino acids will leave the reshaped V-regions resembling the surface character of a truly human antibody. Therefore, it can be argued that antibodies humanized by the above methods may be immunogenic in man.

35 Antigenicity of Antibodies

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[0015] The antigenicity/immunogenicity of an antibody, including recombinant reshaped antibody products, introduced into humans can be viewed as a surface phenomenon. In general one can view the immune system as scanning the surface of a protein introduced to the body. If the F_{ν} portion of a humanized antibody 'opens-up' in the circulation then internal residues can be presented to the immune system. On the other hand, if the F_{ν} portion is stable and tightly packed then only the surface residues presented by the V-regions and the interface between the V_L and V_H regions will be 'scanned'.

Surface Reshaping or Resurfacing of Antibodies

[0016] The notion of surface presentation of proteins to the immune system raises the prospect of redesigning murine monoclonal antibodies to resemble human antibodies by humanizing only those amino acids that are accessible at the surface of the V-regions of the recombinant F_v. The resurfacing of murine monoclonal antibodies to reduce their immunogenicity could be beneficial in maintaining the avidity of the original monoclonal antibody in the reshaped version, because the natural framework-CDR interactions are retained. The value of maintaining the integrity of the framework-CDR interactions has been illustrated as summarized below.

[0017] In a recent research report, two different reshaped versions of the rat monodonal antibody, Campath-9 (antihuman CD4), were generated (Gorman, S.D., Clark, M.R., Routledge, E.G., Cobbold, S.P. and Waldmann, H. (1991), Proc. Natl. Acad. Sci. U.S.A. 88, pp. 4181-4185). In one version, pV_HNEW/C_{G1}, the acceptor V_H framework was from the human NEW-based heavy chain, which has 47% identical residues to the Campath-9 V_H. While in the second version, pV_HKOL/C_{G1}, the acceptor V_H framework was from the human KOL antibody, which has 72% identical residues to Campath-9 V_H. Each reshaped antibody contained the identical V_L domain from the human REI antibody sequence. However, the recombinant product of pV_HKOL/C_{G1} had an avidity for CD4 that was substantially greater than the

product of pV_HNEW/C_{G1}. The authors proposed a reshaping strategy where human sequences, that are highly homologous to the rodent antibody of interest, are transferred, by in vitro mutagenesis, into the rodent V-region to create a "bestfit" reshaped antibody. This strategy uses the term "bestfit" to describe the modeling process, however, there is no quantitative formula employed to assess "bestfit", and so in effect, the process is subjective. Additionally, there is no resurfacing concept presented in that paper.

[0018] The concept of reducing rodent-derived antibody immunogenicity through the replacement of exposed residues in the antibody framework regions which differ from those of human origin is discussed in a recent paper (Padlan, E.A. (1991), Molecular Immunology 28, pp. 489-498). In that paper, the variable domains of two antibody structures, KOL (human) and J539 (mouse), are examined. The crystal structures of the Fab fragments of these two antibodies have been elucidated to high resolution. The solvent accessibility of the exposed framework residues in the variable domains of these two antibodies were compared to a sequence database of human and murine antibody V-region subgroups. On the basis of his findings, Padlan proposed to reduce the antigenicity of allogeneic variable domains [murine V-regions], through replacement of the exposed residues in the framework regions with residues usually found in human antibodies. In murine sequences with the highest similarity to a given human sequence, the number of changes necessary to "humanize" a murine V-region surface would range from 6-15 amino acid changes per V-region. This reference suggests how to convert one antibody surface into another but no general method is developed. Application of the procedure is provided by two examples, a worst-case and a best-case.

Worst Case:

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[0019] Among the representative murine kappa V_L sequences examined for which its autologous V_H has been sequenced, S107 V_L has the most residues that need to be replaced to humanize it. S107 V_L is most similar to the members of the human subgroup VKIV and JK2. The exposed or partially exposed residues that need to be replaced are those at positions 9, 10, 14, 15, 16, 17, 18, 22, 41, 63, 80, 83, 85, 100 and 106. Murine V-region S107 V_H is most similar in its framework to the members of the human subgroup VHIII and JH6. The exposed or partially exposed residues in S107 V_H that need to be replaced are those at positions 3, 40, 68, 73, 75, 76, 82b and 89. A total of 23 residues need to be replaced to humanize the variable domains of S107.

Best Case:

[0020] Among the murine V_H sequences examined for which the autologous V_L has also been sequenced, MOPC21 V_H has the least number of residues that need to be replaced to humanize it. MOPC21 V_H is most similar in its framework to the members of the human subgroup HIII and JH6. The exposed or partially exposed residues that need to be replaced are those at positions 1, 42, 74, 82a, 84, 89 and 108. MOPC21 V_L is most similar in its framework to human subgroup VKIV and JK4. The exposed or partially exposed residues that need to be replaced are those at positions 1, 9, 12, 15, 22, 41, 63, 68, 83 and 85. A total of 17 amino acids need to be replaced to humanize the variable domains of MOPC21.

[0021] Of the light chains in the Best- and Worst-Case examples cited above, S107V_L required changes at 15 positions and MOPC21V_L required changes at 10 positions. Only seven of the changes are common to both of these light chain sequences (see underlined residues). Moreover, of the heavy chain residues that need to be replaced to humanize the respective V-regions, S107V_H required changes at 8 positions and MOPC21V_H required changes at 7 positions. In this instance, only one position is common to both of these heavy chain sequences (see residues in boldface).

[0022] An analysis of S107 V-regions alone would not have led to the prediction of which residues to change in

MOPC21. The reason for this is that the surface residues in Padlan's analysis are only determined by reference to the crystal structure analysis of <u>one</u> antibody. In addition, the basis for defining the surface exposure of an amino acid at a particular position on that crystal structure is a continuous gradient of change, e.g., the fractional solvent accessibility values (Padlan, E.A. (1990), Molecular Immunology 28, pp. 489-498) were computed, where: 0 to 0.2 = completely buried, 0.2 to 0.4 = mostly buried, 0.4 to 0.6 = partly buried/partly exposed, 0.6 to 0.8 = mostly exposed, and 0.8 or above = completely exposed. By limiting the analysis of exposed surface residues to a single crystal structure and by superimposing a broad range of solvent accessibility ratios on exposed residues, such a modeling strategy could be expected to have a wide margin of error in its calculations. This model fails to take into account the great majority of structural information available in the database for other antibody crystal structures.

SUMMARY OF THE INVENTION

[0023] Accordingly, it is an object of this invention to provide humanized rodent antibodies or fragments thereof, and in particular, humanized rodent monoclonal antibodies that have improved therapeutic efficacy in patients due to the presentation of a human surface on the V-region. This and other objects have been attained by providing a method of

producing paired peptides which may or may not be covalently bonded via a disulfide bond or peptide linker, and which comprise humanized heavy and light chains of a rodent antibody variable region, said method comprising:

- (a) generating sequence alignments, in framework positions only, from relative accessibility distributions from x-ray crystallographic structures of a pool of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions;
- (b) defining for a rodent antibody variable region a set of heavy and light chain surface exposed amino acid residues using said set of surface exposed framework positions generated in said step (a);
- (c) identifying from human antibody amino acid sequences a set of variable region heavy and light chain surface exposed amino acid residues that is most closely identical to said set of rodent surface exposed amino acid residues defined in said step (b), wherein said heavy and light chains from said human antibody are or are not naturally paired;
- (d) substituting, in the amino acid sequence of said rodent variable region, said set of heavy and light chain surface exposed amino acid residues defined in said step (b) with said human set of heavy and light chain surface exposed amino acid residues identified in said step (c);
- (e) constructing three-dimensional models of said variable region of said rodent antibody and of said variable region of said rodent antibody resulting from the substituting specified in said step (d);
- (f) comparing said three-dimensional models constructed in said step (e) and identifying any amino acid residues from said sets identified in said steps (b) and (c) that are close to any atom of any residue of the complementarity determining regions of said rodent variable region:
- (g) changing any residues identified in said step (f) from the human to the original rodent amino acid residue to thereby define a humanizing set of surface exposed amino acid residues;
- (h) replacing the set of rodent antibody variable region surface exposed amino acid residues defined in said step
- (b) with the humanizing set of surface exposed amino acid residues defined in said step (g); and
- (i) producing said paired peptides,

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wherein in step (a) sequence alignments are generated from a sufficient number of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions wherein said set is identical in at least about 98% of said sequence alignment positions and in that in step (f) amino acid residues from said sets identified in said steps (b) and (c) that are within 5x10⁻¹⁰m (5 Ångstroms) of any atom of any residue of the complementarity determining regions of said variable region to be humanized are identified.

[0024] Also provided is a method of producing a humanized rodent antibody or fragment thereof by resurfacing, said method comprising:

- (a) generating sequence alignments, in framework positions only, from relative accessibility distributions from x-ray crystallographic structures of a pool of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions;
 - (b) defining for a rodent antibody or fragment thereof a set of variable region heavy and light chain surface exposed amino acid residues using said set of surface exposed framework positions generated in said step (a);
 - (c) identifying from human antibody amino acid sequences a set of variable region heavy and light chain surface exposed amino acid residues that is most closely identical to said set of rodent surface exposed amino acid residues defined in said step (b), wherein said heavy and light chains from said human antibody are or are not naturally paired;
 - (d) substituting, in the amino acid sequence of said rodent antibody or fragment thereof, said set of heavy and light chain surface exposed amino acid residues defined in said step (b) with said human set of heavy and light chain surface exposed amino acid residues identified in said step (c);
 - (e) constructing three-dimensional models of said variable region of said rodent antibody or fragment thereof and of said variable region of said rodent antibody or fragment thereof resulting from the substituting specified in said step (d);
- (f) comparing said three-dimensional models constructed in said step (e) and identifying any amino acid residues from said sets identified in said steps (b) and (c) that are close to any atom of any residue of the complementarity determining regions of said rodent antibody or fragment thereof;
 - (g) changing any residues identified in said step (f) from the human to the original rodent amino acid residue to thereby define a humanizing set of surface exposed amino acid residues;
- (h) replacing the set of rodent antibody surface exposed amino acid residues defined in said step (b) with the humanizing set of surface exposed amino acid residues defined in said step (g); and
 - (i) producing said humanized antibody or fragment thereof;

wherein in step (a) sequence alignments are generated from a sufficient number of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions wherein said set is identical in at least about 98% of said sequence alignment positions and in that in step (f) amino acid residues from said sets identified in said steps (b) and (c) that are within 5x10⁻¹⁰m (5 Ångstroms) of any atom of any residue of the complementarity determining regions of said rodent antibody or fragment thereof to be humanized are identified.

[0025] In a preferred embodiment, the rodent antibody or fragment thereof is a murine antibody, and most preferably murine antibody N901.

BRIEF DESCRIPTION OF THE FIGURES

[0026]

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Figure 1 shows an algorithm that can be used for constructing a three-dimenensional model of the rodent antibody variable region.

Figure 2 is a diagram showing the approach to determine how to humanize a rodent antibody or fragment thereof according to the present invention.

Figures 3A and 3B are plots of relative accessibility of amino acid residues for twelve antibody F_v structures, mapped onto the sequence alignment of these structures. Structures Glb2 (Jeffrey, P.D., Doctor of Philosophy Thesis, University of Oxford, United Kingdom, 1991), D1.3 (Amit, A.G., Mariuzza, R.A., Phillips, S.E.V. and Poljak, R.J. (1986), Science 233, pp. 747-753), 3D6 (Grunow, R., Jahn, S., Porstman, T., Kiessig, T., Steinkeller, H., Steindl, F., Mattanovich, D., Gurtler, L., Deinhardt, F., Katinger, H. and von R., B. (1988), J. Immunol. Meth. 106, pp. 257-265) and 36-71 (5fab) (Rose, D.R., Strong, R.K., Margolis, M.N., Gefter, M.L. and Petsko, G.A. (1990), Proc. Natl. Acad. Sci. U.S.A. 87, pp. 338-342) are not yet present in the Brookhaven database. The other structures used were: 2hfl (Sheriff, S., Silverton, E.W., Padlan, E.A., Cohen, G.H., Smith-Gill, S.J., Finzel, B.C. and Davies, D.R. (1987), Proc. Natl. Acad. Sci. U.S.A. 84, pp. 8075-8079), 3hfm (Padlan, E., Silverton, E., Sheriff, S., Cohen, G., Smith-Gill, S. and Davies, D. (1989), Proc. Natl. Acad. Sci. U.S.A. 86, pp. 5938-5942), 2fbj (Mainhart, C.R., Potter, M. and Feldmann, R.J. (1984), Mol. Immunol. 21, pp. 469-478), 3fab (Saul, F.A., Amzel, L.M. and Poljak, R.J. (1978), J. Biol. Chem. 253, pp. 585-597), 4fab (Herron, J., He, X., Mason, M., Voss, E. and Edmunson, A. (1989), Proteins: Struct., Funct., Genet. 5, pp. 271-280), 2mcp (Segal, D., Padlan, E., Cohen, G., Rudikoff, S., Potter, M. and Davies, D. (1974), Proc. Natl. Acad. Sci. U.S.A. 71, pp. 4298), 2fb4 (Marquart, M. Deisenhofer, J. and Huber, R. (1980), J. Mol. Biol. 141, pp. 369-391), and 1f19 (Lascombe, M. Alzari, P., Boulot, G., Salujian, P., Tougard, P., Berek, C., Haba, S., Rosen, E., Nisonof, A. and Poljak, R. (1989), Proc. Natl. Acad. Sci. U.S.A. 86, p. 607). These structures are designated by their Brookhaven entry code. The sequence numbering used here is described in Figures 4A and 4B. Figure 3A graphically shows the relative accessibility for the heavy chain and Figure 3B graphically shows the relative accessibility for the light chain.

Figures 4A and 4B show alignments of sequences generated using the three methods of humanization. Sequences are: 1) Original rodent N901. 2+3) KOL (Marquart, M. Deisenhofer, J. and Huber, R. (1980), J. Mol. Biol. 141, pp. 369-391) and reshaped N901 using KOL surface. 4+5) Most homologous sequences, L(KV2F) (Klobeck, H., Meindl, A., Combriato, G., Solomon, A. and Zachau, H. (1985), Nucleic Acids Res. pp. 6499-6513) and H(G36005) (Schroeder, H. and Wang, J. (1990), Proc. Natl. Acad. Sci. U.S.A. 87), and reshaped N901 using these sequences. 6+7) Most homologous with respect to surface residues, L(KV4B) (Klobeck, H., Bronkamp, G., Combriato, G., Mocikat, R., Pohelnz, H. and Zachau, H. (1985), Nucleic Acids Res. 3, pp. 6515-6529) and H(PLO123) (Bird, J., Galili, N., Link, M., Sites, D. and Sklar, J. (1988), J. Exp. Med. 168, pp. 229-245), and reshaped N901 using these sequences. The numbering is the same as used in the antibody modelling program ABM (trademark for commercial software, Oxford Molecular Ltd., Oxford, U.K.), which is based on structural conservation and not sequence homology as used by Padlan et al. (Kabat, E.A., Wu, T.T., Reid-Miller, M., Perry, H.M. and Gottesman, K.S. (1987), Sequences of Proteins of Immunological Interest. U.S. Department of Health and Human Services, Fourth Edition). The sequence changes which have to be introduced in order to resurface N901 with a given sequence are marked with bars, back-mutations as determined from F_v models are marked with stars. The sequence homology of given sequences to N901 are shown in brackets after each sequence.

Figure 5 is a stereo plot of mean antibody β -barrel, coordinates determined by iterative multiple fitting of eight antibody structures. Strands 7 and 8 comprise the 'take off' positions for CDR H3 and are not included in the fitting of V_L and V_H regions.

Figure 6 is a plot of RMS deviation from the mean of the eight β -sheet strands comprising the framework. The RMS was calculated from structures F19.9, 4-4-20, NEW, FBJ, KOL, HyHEL-5, HyHEL-10 and McPC603. N,C α , C atoms are included in the plot. The residues used are shown in the alignment (Table 2). The most disordered residues are all the residues of strand HFR4, the last residue of LFR1, and the first and last residue of HFR2. The nomenclature of the strands is explained in the alignment in Table 2. LFR1 - #1, LFR2 - #2, LFR3 - #3, LFR4 - #4,

HFR1 - #5, HFR2 - #6, HFR3 - #7, HFRS4 - #8.

Figure 7 is a flowchart of the overall modelling protocol known as CAMAL.

Figure 8 is a plot of superimposed loop backbones for models and x-ray structures discussed in Example 2. The loops are positioned after global framework fit. This does not represent the best local least squares fit, but shows how the loops are positioned globally onto the framework.

Figures 9A to 9D are stereo (N,C- α ,C,O) representations of crystal structures and models of D1.3, 3671 and Gloop-2 variable domain and β -barrel strands described in Example 2. Crystal structures are shown with open bonds, model with solid bonds. The difference between the 3D6-H3 in the model and the crystal structure is due to a 5-7° twist in the extended β -sheet conformation of this loop, Figure 9A: D1.3, Figure 9B: 36-71, Figure 9C: Gloop-2, Figure 9D: 3D6.

Figure 10 is a histogram showing the distribution of loop length for CDR H3 loops, data from Kabat et al. (Kabat, E.A., Wu, T.T., Reid-Miller, M., Perry, H.M. and Gottesman, K.S. (1987), Sequences of Proteins of Immunological Interest. U.S. Department of Health and Human Services, Fourth Edition).

15 DETAILED DESCRIPTION OF THE INVENTION

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[0027] The existence of specific, yet different, surface patches in murine and human antibodies may be the origin of the inherited immunogenicity of murine antibodies in humans. Statistical analysis of a database of unique human and murine antibody F_v fragments has revealed that certain combinations of residues in exposed surface positions are specific for human and murine sequences. The combinations are not the same in human and murine F_v domains. However, it is possible to define families of surface residues for the two species of antibodies. These families reveal a novel method for the "humanization" or reshaping of murine antibodies. Humanization is the modification of the solvent accessible surface of a non-human antibody or fragment thereof to resemble the surface of a chosen human antibody or fragment thereof such that the modified non-human antibody or fragment thereof exhibits lower immunogenicity when administered to humans. Such a process applies in the present application to antibody variable regions but could equally well apply to any other antibody fragment. The method is considered to be generally applicable to humanization of rodent antibodies.

[0028] According to the present invention, a statistical analysis is presented which is based on accessibility calculated for a range of antibody crystal structures. When this information is applied to an antibody sequence database, it is possible to discriminate between human and murine antibodies at the sequence level purely on the basis of their surface residue profiles.

Rational Resurfacing Approach

- 35 [0029] There are several key features of the resurfacing approach of the present invention.
 - 1) This method uses as a starting point, construction of a three-dimensional model of a rodent variable region by known methods:
 - 2) A large number (e.g., twelve) of antibody F_v or Fab fragment x-ray crystallographic structures are analyzed to produce an unambiguous set of surface exposed amino acid residues that will be positionally identical for a majority (98%) of antibodies. The set is produced by identifying all those residues whose solvent accessibility is above a given cut-off (typically 30%), calculated using a modification of the method of Kabsch and Sander (Kabsch, W. and Sander, C. (1983), Biopolymers 22, pp. 2257-2637) in which explicit atomic radii are used for each atom type to predict sidechain positions as is described below in more detail;
 - 3) Using a complete human antibody database, the best set of human heavy and light chain surface exposed amino acid residues is selected on the basis of their closest identity to the set of surface amino acid residues of the murine antibody;
 - 4) In order to retain the conformational structure of the CDRs of the rodent antibody, replacement of any human surface exposed amino acid with the original rodent surface exposed amino acid residue is carried out whenever a surface residue is calculated from the three-dimensional model to be within 5 Angstroms of a CDR residue.

[0030] The general resurfacing approach of the present invention is illustrated in Figure 2. The approach can be divided into two stages. In the first, the rodent framework (white) is retained and only the surface residues changed from rodent (dark grey circles) to the closest human pattern (light grey circles). This should remove the antigenicity of the rodent antibody. In the second stage, surface residues within 5x10⁻¹⁰m (5 Angstroms) of the CDRs are replaced with the rodent equivalents in an attempt to retain antigen binding and CDR conformation.

[0031] The method of the present invention is applicable to whole antibodies as well as antibody fragments. Suitable antibody fragments that can be used can readily be determined by the skilled artisan. Examples of some suitable

fragments include a single chain antibody (SCA), an antibody F_v fragment, Fab fragment, Fab fragment, Fab fragment, Fab' fragment, or other portion of an antibody comprising the binding site thereof.

[0032] According to the present invention, an important step in the method for determining how to modify a rodent antibody or fragment thereof by resurfacing is to determine the conformational structure of the variable region of the rodent antibody or fragment thereof to be humanized by constructing a three-dimensional model of the rodent antibody variable region. This can be done by known methods such as those described, for example, in Martin et al. (Martin, A. C.R., Cheetham, J.C. and Rees, A.R. (1989), Proc. Natl. Acad. Sci. U.S.A. 86, pp. 9268-9272; Methods in Enzymology (1991), 203, pp. 121-152) and as described in detail in Example 2.

[0033] Martin et al. describe an algorithm which is depicted in Figure 1. The algorithm applies to murine and human antibodies equally well. The present inventors therefore expect that, based on sequence similarity between antibodies of different species (Kabat, E.A. Segments of Proteins of Immunological Interest, National Institutes of Health, U.S.A. 1991), the algorithm will work equally well for rat and other rodent antibodies.

[0034] Briefly, the algorithm depicted in Figure 1 can be summarized as follows. The framework region of an antibody to be modelled is selected on the basis of sequence homology and constructed by a least squares fit onto the six conserved strands of the variable region β-barrel. Light and heavy chain complementarity determining regions are constructed using a combination of canonical structures (Chothia, C. and Lesk, A.M. (1987), J. Molec. Bio. 196, pp. 901-917), database searching and conformational searching. Detailed descriptions of these methods are described in Example 2 herein and in the above two references (Martin et al. 1989 and 1991).

[0035] According to the present invention, another three-dimensional model is also constructed. The other three-dimensional model is of the rodent antibody variable region having human antibody surface amino acid residues substituted therein at particular rodent antibody surface residue positions.

[0036] This other three-dimensional model is constructed by carrying out the series of steps described next.

[0037] The first of the steps is to generate sequence alignments from relative accessibility distributions from x-ray crystallographic structures of a sufficient number of antibody variable region heavy and light chains to give a set of framework positions of surface exposed amino acid residues which is identical in a majority (98%) of the variable regions.

[0038] As used herein, the term "framework" means the antibody variable region from which the complementarity determining regions have been excluded.

[0039] "Complementarity determining regions" means those amino acid sequences corresponding to the following numbering system as defined by Kabat, E.A. (In Sequences of Immunological Interest, N.I.H., U.S.A., 1991).

Light Chain L1 residues 24-34 Light Chain L2 residues 50-56 Light Chain L3 residues 89-97 H1 residues 31-358 Heavy Chain 50-58 Heavy Chain H2 residues Heavy Chain НЗ residues 95-102

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[0040] A sufficient number of rodent antibody fragments that need to be analyzed in order to produce the set of framework positions of surface exposed amino acid residues can readily be determined by the skilled artisan through routine experimentation using a database of antibody sequences. Thus, this step can be conducted using suitable databases now in existence or later compiled.

[0041] The x-ray crystallographic structures are used to determine relative accessibility distributions of surface exposed amino acid residues. The relative accessibility distributions identify all those residues whose solvent accessibility is above a given cut-off (typically 30%), calculated using a modification of the method of Kabsch and Sander (Kabsch, W. and Sander C. (1983), Biopolymers 22, pp. 2257-2637) in which explicit atomic radii are used for each atom type.

[0042] The relative accessibility distributions determined from the x-ray crystallographic structures can then be used to generate sequence alignments which give a set of framework positions of surface exposed amino acid residues which is identical in a majority (98%) of the variable regions.

[0043] The set of framework positions of surface exposed amino acid residues for the variable regions of murine antibodies is shown in Table 1, set forth in Example 1, and was produced using the sequence alignments and accessibility distributions shown in Figures 3A and 3B.

[0044] Once a set of framework positions of surface exposed amino acid residues for the variable regions of the rodent antibodies have been generated, the surface exposed residues of the heavy and light chain pair of the rodent antibody, or fragment thereof, to be humanized can be identified using an alignment procedure such as that described in Example 1 and shown in Figures 3A and 3B. This defines a set of surface exposed amino acid residues of a heavy and light chain pair of a rodent antibody or antibody fragment to be humanized.

[0045] Next, a complete human antibody sequence database is used to identify a set of surface exposed amino acid residues from a human antibody variable region that have the closest positional identity to the set of surface exposed amino acid residues of the variable region of the rodent antibody that is to be humanized. The set of surface exposed

amino acid residues from the human antibodies can be separately identified for a heavy chain and for a light chain that are not naturally paired and/or a set can be identified from a natural human heavy and light chain pair, that is, a pair originating from a single B cell or hybridoma clone. Preferably, the set is one from a natural human heavy and light chain pair.

[0046] A humanized rodent antibody that gives the appearance of a human antibody is then predicted by substituting the set of surface exposed amino acid residues from the rodent antibody or fragment thereof to be humanized with the set of surface exposed amino acid residues from the human antibody.

[0047] A three-dimensional model can then be constructed from the resulting, fully substituted variable region of the rodent antibody or fragment thereof. The three-dimensional model is constructed using the same known methods mentioned above for constructing a 3-D model of the original rodent antibody or fragment thereof.

[0048] While the antigenicity of this fully "resurfaced" or humanized antibody should be removed, an additional factor to be addressed is the binding affinity or the binding strength of the resurfaced antibody. Changes in the framework of the variable domain introduced through resurfacing can influence the conformation of the CDR loops and therefore antigen binding of the antibody. According to the present invention, this problem is removed by the next step which is to identify, by means of a comparison of both of the above-described three-dimensional models of the rodent antibody variable region, any residues from the set of surface exposed amino acid residues of the variable region heavy and light chain pair of the human antibody identified that are within 5 Angstroms of any atom of any residue of the rodent antibody or antibody fragment complementarity determining regions (CDRs).

[0049] Any residue(s) so identified is then changed back from the human to the original rodent amino acid residue(s). [0050] The results of this method can then be applied to a particular rodent antibody by well known methods. Briefly, genes for the humanized variable heavy and light chain regions are constructed using standard recombinant DNA methods (Sambrook, J., Fritsch, E.F. and Maniatis, T. (1989), Molecular Cloning, Second Edition). For example, a PCR method can be used (Daugherty et al. (1991), Nucleic Acids Research 19, pp. 2471-2476).

[0051] Variable heavy chain or variable light chain gene constructs are subcloned into appropriate expression vectors. Suitable expression vectors contain either a human gamma or human kappa constant region gene, a suitable promoter, a sequence coding for a human immunoglobulin leader peptide (for example: met-gly-trp-ser-cys-ile-ile-leu-phe-leu-val-ala-thr-ala-thr (SEQ ID NO:39), Olandi et al. (1989), PNAS 86, pp. 3833-3837), and a drug selectable marker.

[0052] Heavy and light chain expression plasmids can be co-transfected, for example, by electroporation into suitable cells, for example, SP2/0 cells, and selected with an appropriate drug, G418, for example. Screening for intact antibody can be accomplished by ELISA assay. 96-well plates are coated with, for example, goat anti-human kappa chain antibody, and light chains are detected with, for example, goat anti-human antibody conjugated to alkaline phosphatase. [0053] As another approach, light chain constructs are transfected, for example, by electroporation into suitable cells, for example, SP2/0 cells and selected, for example, in hygromycin. Screening for light chain expression can be accomplished by ELISA assay. 96-well plates are coated with, for example, goat anti-human kappa chain antibody, and light chains are detected with, for example, goat anti-human antibody conjugated to alkaline phosphatase.

[0054] A light chain producing line is then used as a host to electroporate in the heavy chain construct. The heavy chain plasmid is co-transfected with a plasmid containing the gene coding for another drug marker, for example, neomycin resistance and selected in the presence of the drug G418. Screening for intact antibody is accomplished by ELISA assay. 96-well plates are coated with, for example, goat anti-human Fc and detected with, for example, goat anti-human light chain conjugated to alkaline phosphatase.

EXAMPLE 1 AND COMPARATIVE EXAMPLES

[0055] The superiority of the presently claimed method for determining how to modify a rodent antibody or fragment thereof by resurfacing in order to produce a humanized rodent antibody will now be described by reference to the following example and comparative examples which are illustrative and are not meant to limit the present invention.

A) Analysis for Murine Antibodies

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[0056] In order to determine the positions which are usually accessible on the surface of the F_{ν} domain of murine antibodies, the accessibility was calculated for twelve Fab x-ray crystallographic structures obtained from the Brookhaven database (Bernstein, F., Koetzle, T., Williams, G., Meyer, E., Brice, M., Rodgers, J., Kennard, O., Shimanouchi, T. and Tasumi, M. (1977), J. Mol. Biol. 112, pp. 535-542). The relative accessibility was calculated using the program MC (Pedersen, J. (1991)), which implements a modified version of the DSSP (Kabsch, W. and Sander, C. (1983), Biopolymers 22, pp. 2257-2637) accessibility calculation routine in which explicit atomic radii are specified for every atom. A residue was defined as being surface accessible when the relative accessibility was greater than 30%. The alignment positions of these residues were conserved in all twelve structures (98% identity). Surface accessions

sible framework positions constitute 40% of the F_v surface area. The remaining surface accessible residues are in the CDRs and in the interdomain C-terminal region. Figures 3A and 3B show a sequence alignment of the twelve crystal structures, the average relative accessibility, and the 30% accessibility cutoff. Figure 3A shows the alignments relative accessibility for the twelve antibody light chains and Figure 3B shows the alignments and relative accessibility for the antibody heavy chains.

[0057] The surface accessible framework positions were mapped onto a database of unique human and mouse F_{ν} sequences (see lists at the end of this Example). The frequency of particular residues in each of these positions is shown in Table 1. Only residue frequencies higher than 5% are listed.

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Table 1:

Distribution of accessible residues in murine and human V_H and V_L chain sequences. All of the positions appear to be conserved which leads to the hyphothesis that immunogenecity arises from a specific combination of these surface residues. The sequence numbering is explained in Figures 3A and 3B.

	surface residues. The sequence numbering is explained in Figures 3A and 3B.							
15		Light chain	·					
	Position	Human	Mouse					
	1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6					
	3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5					
20	5	T 61 L 37	T 87					
	9	P 26 S 26 G 17 A 14 L 7	S 36 A 29 L 17 P 5					
	15	P 62 V 25 L 12	L 47 P 30 V 8 A 7					
	18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9					
	46	P 94	P 82 S 9					
25	47	G 89	G 71 D 18					
	51	K 43 R 31	K 70 Q 13 R 8 T 5					
	63	G 91	G 98					
	66	D 43 S 25 A 9	D 38 A 26 S 26					
30	73	S 96	S 90 I 5					
	76	D 43 T 18 S 16 E 15	D 67 S 15 A 5 K 5					
	86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6					
	87	E 71 D 11 G 7	E 91 D 6					
	111	K 74 R 12 N 6	K 93					
35	115	K 54 L 40	K 87 L 5					
	116	R 60 G 33 S 5	R 89 G 9					
	117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5					
		Heavy chain						
40 .	Position	Human	Mouse					
	118	E 47 Q 46	E 59 Q 29 D 10					
	120	Q 83 T 7	Q 68 K 26					
	122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5					
45	126	G 54 A 23 P 18	G 36 P 30 A 29					
	127 .	G 53 E 22 A 14 D 7	E 45 G 43 S 6					
	128	L 61 V 31 F 7	L 96					
	130	K 46 Q 41 E 5	K 52 Q 27 R 17					
50	131	P 95	P 91 A 5					
50	132	G 74 S 16 T 7	G 82 S 17					
	136	R 53 K 23 S 17 T 7	K 66 S 17 R 13					
	143	G 96	G 98					
	145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5					
55	160	P 84 S 10	P 89 H 7					
	161	G 93	G 71 E 24					
	162	K 76 Q 10 R 8	K 50 Q 30 N 10 H 5					

Table 1: (continued)

Distribution of accessible residues in murine and human V_H and V_L chain sequences. All of the positions appear to be conserved which leads to the hyphothesis that immunogenecity arises from a specific combination of these surface residues. The sequence numbering is explained in Figures 3A and 3B.

		Heavy chain	•
	Position	Human	Mouse
10	183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11
	184	S 70 K 9 P 8	K 42 S 37 T 6
	186	K 53 Q 22 R 7 N 5	K 83 Q 7
	187	G 66 S 21 T 5	G 62 S 18 D 10
	195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6
	196	S 91	S 76 A 16
15	197	K 65 I 8 T 8 R 5	S 46 K 34 Q 11
	208	R 46 T 18 K 17 D 6	T 55 R 26 K 8
	209	. A 50 P 21 S 13 T 8	S 67 A 14 T 11
	210	E 46 A 18 D 13 S 9 Z 8 V 5	E 88 D 7
20	212	T 91	T 53 S 43
	222	G 17 D 11 P 10 Y 9 V N 8	D 67 A 18

[0058] None of the entire combinations of surface residues in the human sequences are found in the murine sequences and *vice versa* (see lists at the end of this Example). However, the residues in individual positions appear to be conserved (see Table 1). There are few residues which differ significantly between the species; these are at positions 54 and 91 of the L chain and 168 and 216 of the H chain. Of these positions only position 216 is a non conservative (V to Y) mutation. Differences between human and murine antigenicities are therefore believed to arise from the combinations of residues in these positions.

[0059] In order to determine whether the mouse sequences are more distantly related to human F_v sequences than to other mouse F_v sequences, the homology was calculated using a Dayhoff mutation matrix (Dayhoff, M., Barker, W. and Hunt, L. (1983), Meth. Enz. 91, pp. 524-545). The homology was calculated between all the sequences in a pool of both human and mouse sequence patches made up of the surface accessible residues. The data was then represented as a density map (not shown) in which the sequences are plotted against each other. The density map can be used to discriminate "murine surfaces" from "human surfaces".

B) Reshaping of Antibody N901

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[0060] In order to test the resurfacing approach suggested by the above analysis, three humanization experiments were set up. 1) Traditional loop grafting (Verhoeyen, M.E., Saunders, J.A., Broderick, E.L., Eida, S.J. and Badley, R. A. (1991), Disease markers 9, pp. 3-4) onto a human F_v framework of known structure (KOL). 2) Resurfacing approach using most similar chain. 3) Resurfacing approach using human sequences with most similar surface residues.

[0061] The antibody used was the murine anti-N901 antibody (Griffin et al. (1983), J. Imm. 130, pp. 2947-2951). The anti-N901 antibody (also referred to herein as the "N901 antibody") is available commercially from Coulter Corporation under the name NKH-1.

[0062] The alignment of the light chain sequences and heavy chain sequences in Figures 4A and 4B, respectively, show the original N901 antibody and the sequences used in each of the three approaches outlined here.

[0063] Figures 4A and 4B show alignments of sequences generated using the three methods of humanization. Sequences are: 1) Original rodent N901. 2+3) KOL (Marquart, M. Deisenhofer, J. and Huber, R. (1980), J. Mol. Biol. 141, pp. 369-391) and reshaped N901 using KOL surface. 4+5) Most homologous sequences, L(KV2F) (Klobeck, H., Meindl, A., Combriato, G., Solomon, A. and Zachau, H. (1985), Nucleic Acids Res., pp. 6499-6513) and H(G36005) (Schroeder, H. and Wang, J. (1990), Proc. Natl. Acad. Sci. U.S.A. 87) and reshaped N901 using these sequences. 6+7) Most homologous with respect to surface residues, L(KV4B) (Klobeck, H., Bronkamp, G., Combriato, G., Mocikat, R., Pohelnz, H. and Zachau, H. (1985), Nucleic Acids Res. 3, pp. 6515-6529) and H(PLO123) (Bird, J., Galili, N., Link, M., Sites, D. and Sklar, J. (1988), J. Exp. Med. 168, pp. 229-245), and reshaped N901 using these sequences. The numbering is the same as used in the antibody modelling program ABM (ABM is a trademark for commercial software, Oxford Molecular Ltd., Oxford, U.K.), which is based on structural conservation and not sequence homology as used by Padlan et al. (Kabat, E.A., Wu, T.T., Reid-Miller, M., Perry, H.M. and Gottesman, K.S. (1987), Sequences of Proteins

of Immunological Interest. U.S. Department of Health and Human Services, Fourth Edition). The sequence changes which have to be introduced in order to reshape N901 with a given sequence are marked with bars, and back-mutations as determined from F_v models are marked with stars. The sequence homology of a given sequence to N901 is shown in brackets after each sequence.

(1) Classical Humanization

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[0064] In classical humanization the rationale is to graft the rodent CDR's onto a framework of known structure, such that CDR-framework interactions can be accurately monitored by homology modelling. The model of the humanized antibody is compared to that of the original rodent antibody, and possible CDR interacting framework residues are back mutated (marked with '*' in alignment) in order to retain the three-dimensional shape of the CDR's. In this example the antibody KOL was used, giving a low homology score of only 77 and 46 in the heavy and light chains respectively.

(2) Most Similar Chain Resurfacing

[0065] A database of nonredundant human antibody sequences was compiled from available protein and nucleotide sequences. A total of 164 H and 129 L chains were sampled.

[0066] Each of the rodent chains, L and H, were then matched and the most similar human sequence found independently (G36005/KV2F) (Schroeder, H. and Wang, J. (1990), Proc. Natl. Acad. Sci. U.S.A. 87); Klobeck, H., Meindl, A., Combriato, G., Solomon, A. and Zachau, H. (1985), Nucleic Acids Res., pp. 6499-6513). Surface residues, as outlined in Table 1, were then changed in the rodent sequences to match those of the human sequences. Subsequently a model was built of the resurfaced antibody and compared to the model of the original rodent antibody and back mutation of any CDR interacting residues was performed.

(3) Most Similar Surface Replacement According to the Present Invention

[0067] This method is identical to the above method, except that the similarity is calculated only over the surface residues outlined in Table 1 above.

[0068] The same procedure of surface mutation and subsequent back mutation was performed as in the previous methods. In this case the chosen sequences were PLO123/KV4B (Bird, J., Galili, N., Link, M., Sites, D. and Sklar, J. (1988), J. Exp. Med. 168, pp. 229-245); Klobeck, H., Bronkamp, G., Combriato, G., Mocikat, R., Pohelnz, H. and Zachau, H. (1985), Nucleic Acids Res. 3, pp. 6515-6529).

[0069] The following lists show the surface residue patterns in mouse and human light and heavy chain antibody variable regions. The sequences are ordered on similarity to one another. There are no pattern matches between mouse and human sequences although there are matches within a species.

HOUSE LIGHT CHAIN SURFACE PATCHES

	1	KVSESMOUSE	· YTCI DOCYCCCDUCIOLA	1050	-		
5		PL0101	: KTSLRPGKGSSDYEKK*				40)
		NS1F19L		(SEQ			
		KVSUSHOUSE		(SEQ			.42)
		MUSIGLDD		(SEQ			
•		PL0220		(SEQ			
10		KV5J\$MOUSE		(SEQ			•
10				(SEQ			
		MUSICKABB		(SEQ			•
		MUSIGKCLG		(SEQ			
		MUSIGGVJ2	:QTSLRPDKGKSDSEKK*				49)
		MUSIGKCRN		(SEQ			
15		Musigkclf Musigkacm	: VISLAPGRESSDPERK*	(SEQ			
		MUSIGKABE		(SEQ			•
			:QISLRPGKGSSDSEKK*	(SEQ			
`	15	KV5P\$HOUSE MUSIGKCHK	: QTSLRPGKGDSDEDKK* : ETALRPGKGASDADKK*	(SEQ			
	17	KV3D\$MOUSE	. 1981 1 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	(SEQ			
20		MUSIGRAAW		(SEQ			
		KVJGSHOUSE		(SEQ			
		KVJESHOUSE		(SEQ			
		MUSIGRAAZ	· Author Denace Denace -	(SEQ			
		MUSIGRONE	: GTSLRPDKGSSDQETT* : GNSLTPGKGSSSPEKK*	(SEQ	ID	NO:	60)
25		MUSICKBA	• ————————————————————————————————————	(SEQ	ID	NO:	61)
		KVSASMOUSE		(SEQ			
		MUSICKY		SEQ			
		MUSIGKCNM		SEQ			
		MUSIGKCL1		SEQ			
30		KV5BSMOUSE		SEQ			
,		MUSIGKCSA		SEQ			
				SEQ			
	31	Musigkesk Musigkest	: VTKVRSGKGESDAEKK*	SEQ			
		MUSIGKAB		SEQ			
35		PL0014		SEQ			72)
		MUSICKACU		SEQ			73)
		PS0023		SEQ			74)
		H\$ 2MCPL		SEQ			
		MUSICKADY		SEQ			76)
40		MUSIGRCPF		SEQ			77)
40		MUSICLDB		SEQ			78)
		MUSICKCHE		SEQ			
		B27887		SEQ			
		H28840		SEQ			
45		KV2GSHOUSE		SEQ			
45		C27887		SEQ			
		JL0029		SEQ			
		HUSIGKAEH		SEQ			
		PS0074		SEQ			
		MUSICKCNY		SEQ			
50		MUSIGKCNX		SEQ			
		KV2D\$MOUSE		SEQ			
	-	,,,,					•

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:ESSARPGKGDSDAEKK*
:VTLSSPGQGDSDAEKK*
:VTLSSPGQGDSDAEKK*
:VTTAKPEKGDSDVEKK*
:VTTAKPEKGDSDVEKK*
:VTTPKPDKGDSDVEKK*
(SEQ ID NO: 92)
:VTAPRFGKGASSAEKK*
(SEQ ID NO: 93)
:VTAPRFGKGASSAEKK*
(SEQ ID NO: 94)
:VTAPKPGKGTSSAEKK*
(SEQ ID NO: 95)
:VTAPKPGKGASSAEKK*
(SEQ ID NO: 96)
:VSAPKPGKGASSAEKK*
(SEQ ID NO: 97)
:VTAPKSGKGASSAEKK*
(SEQ ID NO: 97)
:VTAPKSGKGASSAEKK*
(SEQ ID NO: 97)
:VTAPKSGKGASSAEKK*
(SEQ ID NO: 98)
:VTAPKPDKGVSSAEKK*
(SEQ ID NO: 100)
:VTAPKSEKGVSSAEKK*
(SEQ ID NO: 101)
:FTAPKPGKGASSAEKK*
(SEQ ID NO: 101)
:FTAPKPGKGASSAEKK*
(SEQ ID NO: 102)
:VTAPKSGKGASSAEKK*
(SEQ ID NO: 103)
:VTAPKSGKGASSAEKK*
(SEQ ID NO: 104)
:VTAPKSGKGASSAEKK*
(SEQ ID NO: 105)
:VTAPKSGKGASSAEKK*
(SEQ ID NO: 106)
:VTAPKSGKGASSAEKK*
(SEQ ID NO: 106)
:VTLSFGQGNSDAELP*
(SEQ ID NO: 106)
:VTFLSFGQGNSDAELP*
(SEQ ID NO: 108)
:VTLSFFGGSSDEKK*
(SEQ ID NO: 110)
:QTSFTTGKGSSDEKK*
(SEQ ID NO: 110)
:QTSFTTGKGSSDEKK*
(SEQ ID NO: 111)
:QTSFTTGKGSSDEKK*
(SEQ ID NO: 112)
:VTALKSGKGASSAEKK*
(SEQ ID NO: 112)
:VTALKSGKGASSAEKK*
(SEQ ID NO: 113)
:VTALKSGKGASSAEKK*
(SEQ ID NO: 114)
:QTSFTTGKGSSDEKK*
(SEQ ID NO: 112)
:VTALKSGKGASSAEKK*
(SEQ ID NO: 123)
:LLSISFLKGGSDFEKK*
(SEQ ID NO: 124)
:VTAPKSGKGGSSGSEKK*
(SEQ ID NO: 124)
:VTAPKSGKGGSSGSEKK*
(SEQ ID NO: 125)
:VTAPTFDTGAIKTEKL*
(SEQ ID NO: 126)
:AVSPTFDTGAIKTEKL*
(SEQ ID NO: 128)
:AVSPTFDTGAIKTEKL*
(SEQ ID NO: 129)
:AVSPTFDTGAIKTEKL*
(SEQ ID NO: 129)
:AVSPTFDTGAIKTEKL*
(SEQ ID NO: 129)
                                    51 MUSIGRADW
                                   52 KV2A$MOUSE
                                   53 KVIASHOUSE
                                   54 F30534
                                55 MUSIGKCLO
                                  56 G27887
                                  57 MUSIGVKV3
                                  58 MUSIGKCNA
 10
                                  59 S03410
                                  61 PL0013
                                  62 MUSIGLAET
                                  63 MUSIGVKVI
                                  64 KV6KSMOUSE.
                                  65 G30560
                                  66 MUSIGKBO
                                 67 MUSICKCNB
                             68 H33730
69 MUSIGKCPC
20
                                70 KV2C$MOUSE
                                 71 MUSIGLAV
                                72 MUSIGKCNH
                                72 MUSIGRCHH
73 KV5R$MOUSE
74 KV6E$MOUSE
75 MUSIGRCHI
76 MUSIGLDA
77 C26317
                                 77 C26317
                              77 C26317
78 PS0073
79 A23986
80 MUSIGKABW
81 KV5D$NOUSE
82 MUSIGE6L
83 MUSIGKCOE
30
                              84 MUSIGKCKI
85 MUSIGLVD
86 S06822
87 S06821
88 MUSIGLAS
                               90 LV2B$MOUSE
                               91 MUSIGLAN
```

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HUMAN LIGHT CHAIN SURFACE PATCHES

```
:YLPPTPGVIRSTAMKL* (SEQ ID NO: 131)
:YLPPTPGVIRSTAMRL* (SEQ ID NO: 132)
:YLPPTPGLIRSTSMKL* (SEQ ID NO: 133)
:YLPPTPGLIRSTSVKL* (SEQ ID NO: 134)
:YLPPTPGVIRSTAEKL* (SEQ ID NO: 135)
                 1 LV4ASHUMAN
                     2 LV4BSHUMAN
 5
                     3 LV4ESHUMAN
                     4 LV4DSHUMAN
5 LV4CSHUMAN
                                                                       :YLPPTPGVIRSTAGKL* (SEQ ID NO: 135)
:YLPATPGVVRSSAGKL* (SEQ ID NO: 136)
:YLPATPGVVRSSAGKL* (SEQ ID NO: 137)
:SLPPSPGKVRSTAEKL* (SEQ ID NO: 138)
:SLPPSPGKVRSSSEKL* (SEQ ID NO: 140)
:SLPPRPGKVRSSSDKL* (SEQ ID NO: 141)
                     6 LV5ASHUMAN
                     7 LV7ASHUMAN
10
                     8 LV2GSHUMAN
                     9 LV2ISHUMAN
                  10 NS2RHE
                                                                           :SLPPRPGXVRSSDKL*
                                                                                                                                    (SEQ ID NO: 140)
(SEQ ID NO: 141)
(SEQ ID NO: 142)
(SEQ ID NO: 144)
(SEQ ID NO: 145)
                  11 HUMIGLAN
                                                                           :SLPPRPGRVRSSSEKL*
                  12 LV1ASHUMAN
                                                                      :SLPPRPGRVRSSSEKL* (SEQ ID NO: 142)
:SLPPRPGKVRSSSEQL* (SEQ ID NO: 143)
:SLPPRPGKVRSSSETL* (SEQ ID NO: 144)
:SLPPRPGKIRSSTGKL* (SEQ ID NO: 145)
:SLPPRPGRIRSSTGKL* (SEQ ID NO: 146)
:SLPPRPGKIRSSTGQL* (SEQ ID NO: 147)
:SLPPEPGKIRSSTGRL* (SEQ ID NO: 148)
:SLAPSPGKIRSTAEKL* (SEQ ID NO: 149)
:SLPPRPGKIRSSTGN* (SEQ ID NO: 150)
:SLRPSPGKVRSTAEKL* (SEQ ID NO: 151)
:SLRPSPGKVRSTAEKL* (SEQ ID NO: 151)
                  13 LV1B$HUMAN
                 14 LV1PSHUMAN
                  15 LV1CSHUMAN
                  16 A29700
                  17 HUMIGLAN4
                 18 LV1DSHUMAN
20
                 19 LV2KSHUMAN
                 20 LV1ISHUMAN
                 21 LV2E$HUMAN
22 LV2D$HUMAN
23 LV2C$HUMAN
                                                                         :SLRPSPGKVRSTAEKL*
(SEQ ID NO: 151)
:SLRPSPGKVRSTADKL*
(SEQ ID NO: 152)
:SLRPSPGKVRSTAEKL*
(SEQ ID NO: 153)
:SLRPSPGKVRSAVEKL*
(SEQ ID NO: 154)
:SLPPRPGK-RSSAEKL*
(SEQ ID NO: 155)
:SLAPSPGKVRSTVERL*
(SEQ ID NO: 156)
:SLAPSPDKIRSTPDKL*
(SEQ ID NO: 157)
:SLALSPGKVRSTAEKL*
(SEQ ID NO: 158)
:SLPLSAGKVRSTAEKL*
(SEQ ID NO: 160)
:SLPLTPGLIRSTAEKL*
(SEQ ID NO: 161)
:SLPLTPGTDSSSTEKL*
(SEQ ID NO: 162)
25
                 24 LV2J$HUMAN
                 .25 LV1E$HUMAN
                 .26 LV2B$HUKAN
                27 NSINCWW
                .28 LV2H$HUKAN
30
                 29 NS3MCG2 •
                  10 LV2ASHUMAN
                 31 502083
                 32 HUNIGLANS
                                                                                                                             (SEQ ID NO: 162)

(SEQ ID NO: 163)

(SEQ ID NO: 164)

(SEQ ID NO: 165)

(SEQ ID NO: 166)

(SEQ ID NO: 167)

(SEQ ID NO: 168)

(SEQ ID NO: 169)

(SEQ ID NO: 170)

(SEQ ID NO: 171)

(SEQ ID NO: 172)

(SEQ ID NO: 173)

(SEQ ID NO: 174)

(SEQ ID NO: 174)
                                                                       : Fleptpgtdsssterl*
: Fllptpgtdsssterl*
                 33 LV6C$HUMAN
                 34 LV6DSHUMAN
. 35
                                                                          : PLHPTRVTD99STEKL*
                 35 LV6ESHUMAN
                                                                          : Llpptpgtnsssndkl*
                 36 LV6B$HUNAM
                                                                            :VLPLSPHRIRSESENL*
                  37 HUMIGLESG
                                                                           :SLAPSPAKTRSTAERD*
                  38 HUNIGLYC.
                 39 HUNIGVLLS
                                                                           :VTAPRPGRIRSDPEKK+
                                                                           :VTAPRPGRVRSDPEKK*
                 40 HUNIGKAN
                                                                           :VTCPRPCRIRSDPEKK*
                 41 E30609
                                                               :VTGPRPGRIRSDPEKK* (SEQ ID NO: 171)
:VTGPRPGRIRSDPDKK* (SEQ ID NO: 172)
:VTGPRPGRVRSDPEKK* (SEQ ID NO: 173)
:VTGPRPGRIRSDPXKK* (SEQ ID NO: 174)
:VTAPRPGRIRSESERK* (SEQ ID NO: 175)
:VTGPSRGRIRSDPEKK* (SEQ ID NO: 176)
:VTVPRPSRIRSESERK* (SEQ ID NO: 177)
:VTAPGPGRIRSESERK* (SEQ ID NO: 178)
:QTSVRPGRVRSDPEKK* (SEQ ID NO: 179)
:QTSVRPGKVRSDPEKK* (SEQ ID NO: 180)
                 42 XV3B$HUKAN
                 43 G30607
                 44 KV3MSHUKAN
45
                 45 KV3HSHUMAN
                 46 KV3KSHUMAN
              47 KV3FSHUKAN
                48 B26555
                 49 KV1QSHUMAN
              50 KV1W$HUNAM
```

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```
51 KV1MSHUMAN
                                                           (SEQ ID NO: 181)
                                  :QTSVRPGKVRSDPEKK*
        52 KVIRSHUMAN
                                  :QTSVRPGKVRSEPEKK*
                                                           (SEQ ID NO: 182)
        53 KV1F$HUMAN
                                  :QTSVRPGKVRSEPDKK*
                                                           (SEQ ID NO: 183)
5
        54 KV1G$HUMAN
                                  :QTSVRPGKVRAEPEKK*
                                                           (SEQ ID NO: 184)
        55 KV1KSHUMAN
                                  :QTSVRPGKVRSBPZKK*
                                                           (SEQ ID NO: 185)
        56 KVIDSHUMAN
                                  :QTSVRPGKVRSDPBKK*
                                                           (SEQ ID NO: 186)
        57 KV1H$HUMAN
                                  :QTSVRPGQVRSDPERK*
                                                           (SEQ ID NO: 187)
                                                           (SEQ ID NO: 188)
        58 KV1B$HUMAH
                                  :QTSVRPGKVRSHPEKK*
10
        59 B27585
                                  : QTSVRPGNVRSDPDKK*
                                                           (SEQ ID NO: 189)
                                                           (SEQ ID NO: 190)
                                  :QTSVRPGKVRSDPEXT*
        60 NSIREIA
                                  :QTSVRPGTVRSEPEKK*
                                                           (SEQ ID NO: 191)
        61 KV1XSHUMAN
                                  : QTSVRPEKVRSEPDKK*
                                                           (SEQ ID NO: 192)
        62 KVILSHUMAN
                                  : QTSVRPGKVRSESDKK*
                                                           (SEQ ID NO: 193)
        63 IMGL38
15
                                  :QTSVRPGEVRSEPDKK*
                                                           (SEQ ID NO: 194)
        64 A27585
                                  :QTSVRPGBVRSBPZRK*
                                                           (SEQ ID NO: 195)
        65 KVINSHUMAN
                                  : QTSVSPGKVRSDPEKK+
        66 KV1C$HUMAN
                                                           (SEQ ID NO: 196)
        67 KV1V$HUMAN
                                  :QTSVRPGKVNSDPEKK*
                                                           (SEQ ID NO: 197)
        68 KVITSHUMAN
                                  :QTSVRPGKVRSDPDTK*
                                                           (SEQ ID NO: 198)
                                                           (SEQ ID NO: 199)
(SEQ ID NO: 200)
                                  :QTSVRPKKVRSDPZKK*
        69 KV1USHUMAN
20
                                  :QTSVRPKKVRFDPEKK*
        70 KVIASHUMAN
                                  : QTSVRSGKVRSEPETK*
                                                           (SEQ ID NO: 201)
        71 KV1S$HUMAN
                                  :VTNLRPGKVRSDAEKK*
                                                           (SEQ ID NO: 202)
        72 KV4ASHUMAN
                                  : VTDLRPGKVRSDAEKK*
                                                           (SEQ ID NO: 203)
        73 KV4C$HUMAN
                                  :QTSVSPGNIRSESDKK*
                                                           (SEQ ID NO: 204)
        74 HUNIGK2A1
                                  : KTSVTPGKFRSEPEKK*
                                                           (SEQ ID NO: 205)
        75 HUMIGKBA
                                  :VTLLPPGRVRSDAEKK*
                                                           (SEQ ID NO: 206)
        76 HUMIGKBC
                                  :VTLLPPGEVRSDAEKK*
                                                           (SEQ ID NO: 207)
        77 KV2B$HUMAN
                                  :VTLPPPGZVRSDAERK+
                                                           (SEQ ID NO: 208)
        78 KV2DSHUMAN
                                  :VTLPPPGZVRSBAZNK+
                                                           (SEQ ID NO: 209)
        79 KV2C$HUHAN
                                  :VTLPPPQQVRSDAERK*
                                                           (SEQ ID NO: 210)
30
        80 KV2ESHUMAN
                                  :VTLPPPGQVTSDAEKK*
                                                           (SEQ ID NO: 211)
        81 SQ3876 ....
                                  :VTLPPAGQVRSDAERR+
                                                           (SEQ ID NO: 212)
        82 KV2ASHUMAN
                                  :ALSPSSGQSSSASERL+
                                                           (SEQ ID NO: 213)
        83 HUNIGLANS
```

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HOUSE HEAVY CHAIN SURFACE PATCHES

```
: EKVGGLQPGRGTPGKASRGDSQRPES*
                                                                     (SEQ ID NO: 214)
          1 MUSIGHIT
                                                                     (SEQ ID NO: 215)
           MUSIGHIU
                                  : EXVGGLQPGRGTPGKVSRGDSQRPES*
                                  : EKVGGLQPGTGAPGKASRGDSQRPES*
                                                                     (SEQ ID No: 216)
          3 MUSIGHIV
                                                                     (SEQ ID NO: 217)
           MUSIGHYM
                                  : EKVGGLQPGRGTPGKASKGNSQRAES .
                                                                     (SEQ ID NO: 218)
                                  : EKMGGLQPGRGTPGKASKGNSQRAES*
           PU0001
                                                                     (SEQ ID NO: 219)
           MUSIGHFO
                                  : EKVGGLQPGRGTPGKASKGTSQRAES*
                                  : EKVGGLQPGRGTPGKASKGTSQRAET*
                                                                     (SEQ ID NO: 220)
           A30515
                                                                     (SEQ ID NO: 221)
                                  : EKVGGLKPGRGTPGKASKGTSQRAET+
          8 PL0018
10
                                  : ENVGGLQPGRGTPGKASKGTSQRAET+
                                                                     (SEQ ID NO: 222)
           MUSIGHFK
                                                                     (SEQ ID NO: 223)
                                  : EXVGGLQSGRGTPGKASKGTSQRAET+
        10 MUSICHPO
                                                                     (SEQ ID NO: 224)
        11 PU0001
                                  : EXVGGLQSGRGTPGKASKGTSQRAES*
                                  : EKVGGLQPGRGTPGKASKGISQRAER*
                                                                     (SEQ ID NO: 225)
        12 E30540
                                                                     (SEQ ID NO: 226)
         13 HV17SHOUSE
                                  : exvgglqpgrgtpgksakgbszraqs*
                                  : EXVGGLQPGSGTPGKASKGNSQRAES*
                                                                     (SEQ ID NO: 227)
           MUSIGHLN
        14
15
                                  : EKVGGLQPGSGTPGKASKGSSQRAES* .
                                                                     (SEQ ID NO: 228)
         15 MUSIGHKG
                                  : EKVGGLOPGRGTPRKASKGNSQRAES*
                                                                     (SEQ ID NO: 229)
        16 PU0004
                                  : EICKGNLQPGSGTPGKASKGNSQRPDS*
                                                                     (SEQ ID NO: 230)
        17 MUSIGHKJ
                                  : EKVGGLKPGKGTPEKDSKGNARRSET*
        18 HV56SMOUSE
                                                                     (SEQ ID NO: 231)
                                                                     (SEQ ID NO: 232)
(SEQ ID NO: 233)
                                  : EXVGGLXPGKGAPEXDSKGNARRSET*
        19
           C27888
                                  : EXVGGLXPGKGTPERDSKGNARRSET+
        20 MUSIGHAAP
20
                                  : DKVGGLKPGKGTPEKDSKGNAKRSET*
                                                                     (SEQ ID NO: 234)
        21 PH0097
                                  : DKYGGLKPGKGTPEKDSKGNAKKSET+
                                                                     (SEQ ID NO: 235)
        22 E27888
        23 MUSIGHJB
                                  : DKVGGLKPGKGTPDKDNKGNAKKSET+
                                                                     (SEQ ID NO: 236)
                                  : EKVGGLTPGKGTPEKDSKGNGRRSET+
                                                                     (SEQ ID NO: 237)
        24 MUSIGHADL
                                  : ENVGGLKPGKGTPEKDSKGHDRRSET*
                                                                     (SEQ ID NO: 238)
        25 A27888
                                                                     (SEQ ID NO: 239)
                                  : EMVGGLXPGKGTPEXDSKGNDKRSET*
        26 H27887
25
                                                                     (SEQ ID NO: 240)
                                  : ENVGGLKPGKGTPEKDSKGNAKRSET*
        27
           B27888
                                  : BOVGGLEPGKGTPEKDSKGNAKKSET+
                                                                     (SEQ ID NO: 241)
        28 B27889 ·
                                  : BOVGGLKPGKGTPEKDTKGHAKKSET*
                                                                     (SEQ ID NO: 242)
        29 D27889
                                                                     (SEQ ID NO: 243)
                                  : EQVGGLKPGKGAPEKDTKGNAKKSET+
        30. HVS5$MOUSE
                                  : EEVGGLOPGKGTPEKDSKGNAKKSET+
                                                                     (SEQ ID NO: 244)
        31 MUSICHAGT
                                                                     (SEQ ID NO: 245)
                                  : EXVGGLOPGKGTPEXDTKGKAKKSET*
        32 MUSIGVH50
30
                                  : EXVGGLOPGRGTPERDTKGNAKKSET*
                                                                     (SEQ ID NO: 246)
        33 MUSIGHIW
                                                                     (SEQ ID NO: 247)
                                  : EXVGGLOPGKGSPEXDSKGKAKKSET*
        34 MUSICHAGE
                                  : DIOIGGLEPGKGTPEKDSKGHAKQSET*
                                                                     (SEQ ID NO: 248)
        35 PH0098
                                                                     (SEQ ID NO: 249)
                                  : DOVGGLOPGKGTPDKDSKGNAKKSET*
        36 MUSIGHID
                                                                     (SEQ ID NO: 250)
                                  : EXVGGLOPGKGTPEXDSKGKAEKSET*
        37 HUSIGHAGE
                                                                     (SEQ ID NO: 251)
                                   : EQVGDLKPGKGTPEKDTKGHARRSET*
        38 MUSIGHME
35
                                  : ZHVGDLKPGKGAPEKDSKGHARRSET+
                                                                     (SEQ ID NO: 252)
        39 027888
                                  : EQVGGLQPGKGTSDKDSKGNAKKSET*
                                                                     (SEQ ID NO: 253)
        40 MUSIGHIP
                                                                     (SEQ ID NO: 254)
                                   : EQVGGLQPGKGTPEKDSKGNAKKSGT*
        41 NUSIGHAGS
                                  : DOVGGLOPGRGTPERDTRGNPRRSET+
                                                                     (SEQ ID NO: 255)
        42 HV16SMOUSE
                                                                     (SEQ ID NO: 256)
                                  : DQVGGLQPGQGTPEXHTKGHPKRSDT*
        43 834871
                                   : EKVGGLQPGKGTSEKDLKGKAKKSET+
                                                                     (SEQ ID NO: 257)
40
           PH0094
                                                                     (SEQ ID NO: 258)
                                   : DKYGGLKPGKRTPEKDNKGNAKKSET+
         45 PH0096
                                  : DKYGGLILGKGTPEKDTKGHAKKSET*
                                                                     (SEQ ID NO: 259)
           MUSIGVH62
         46
                                                                     (SEQ ID NO: 260)
                                  : EKYGGLOPGKGTPEKDSKGNANTSET*
         47 MUSIGHAGR
                                  : EHVGGLKPGKGTPEKDSKGNAGRSET*
                                                                     (SEQ ID NO: 261)
         48 HV58SMOUSE
                                  : EQVCCLQPCHCTPEXDITCHAKRSET*
                                                                     (SEQ ID NO: 262)
         49 H27888
                                  : Execclopckgtpexeskgdskraft*
                                                                     (SEQ ID NO: 263)
45
         50 HV34SMOUSE
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: EKEGGLQPGKGTPEKESKGDSKRPET*
       51 HV33SHOUSE
                                                                    (SEQ ID NO: 264)
                                : EKEGGLQPGKGSPEKESKGDSKRAET+
       52 MUSIGHZAB
                                                                    (SEQ ID NO: 265)
       53 NS4FABH
                                 : EKDGGLQPGKGTPEKDSKGDSKRVEM+
                                                                   (SEQ ID NO: 266)
                                 : EQVGGLKPGRGTPEXDTTGDAQRSET+
       54 I27888
                                                                    (SEQ ID NO: 267)
                                 : EQVGGLKPGRGTPEKDTTGNAKGSET+
       55 G27888
                                                                    (SEQ ID NO: 268)
                                 : EKVGGSKPGKGTPEKDSKGNAKTSET*
       56 HV59$MOUSE
                                                                    (SEQ ID NO: 269)
       57 MUSIGHOE
                                :SDQGGLKPGKGTPEKDTKGNARRSES+
                                                                    (SEQ ID NO: 270)
       58 NSZFVWH
                                 : EKIGGLQPGKGDPGKPSKDNAKRSET+
                                                                    (SEQ ID NO: 271)
                                 : EKLGGLQPGKGDPGKPSKDNAKRSET•
                                                                    (SEQ ID NO: 272)
       59 MUSIGHIT
                                 : EKLGGLQPGKGDPGKPFKDNAKRSET*
                                                                    (SEQ ID NO: 273)
       60 MUSICHLY
10
      61 506816
                                 : EKLGGLQPGKGDPGKLMKENAKRSET*
                                                                    (SEQ ID NO: 274)
                                 : ENLGGLQPGKGDPGKLKXENAKRPET+
      62 S06817
                                                                    (SEQ ID
                                                                           NO: 275)
      63 MUSICHAAI
                                 : EKLGGLOPGNGDLGKPSKDNAKRSET*
                                                                    (SEQ ID NO: 276)
                                 : EKLGPLQLGKGDPGKPSKDDAKRSET*
       64 HV42$HOUSE
                                                                    (SEQ ID NO: 277)
         MUSIGHAAL
                                 : EQLGGLQPGGGTPGKPSKDNDKRSET+
                                                                    (SEQ ID NO: 278)
                                 : EQLGGLQPGGGTPGKASKDNDKRSET+
         MUSIGHABO
                                                                    (SEQ ID NO: 279)
15
                                 : EQVGGLKARKGTPEKDTTGNAKRSET*
      67 MUSIGHEG
                                                                    (SEQ ID NO: 280)
                                 : ENVGVLEPGKGTPEKRQEGNAKRSET*
      68 MUSICHWN
                                                                    (SEQ ID NO: 281)
                                 : EQVGGLQPKKGSPGKDSKDDSQKTET+
      69 MUSICKCLT
                                                                    (SEQ ID NO: 282)
                                 : EQVGGLQPKKGSPGKDSKDDSQKTER+
      70 MUSIGHZAE
                                                                    (SEQ'ID NO: 283)
                                 : QQVPELKPGRGTPGKEDKGTSARNDT+
      71 MUSIGHAAD
                                                                    (SEQ ID NO: 284)
      72 MUSIGHAAN
                                 : QQVPELKPGKGTPGKDDKGTSAKNET*
20
                                                                    (SEQ ID NO: 285)
      73 MUSIGHAMA
                                 : OQVPZLKPGKGTPGKDDKGTSAKNEM*
                                                                    (SEQ ID NO: 286)
      74 MUSIGHXZ
                                 : QQKPELKPGKGSPGQEKKGTSSTSET*
                                                                    (SEQ ID NO: 287)
                                                                    (SEQ ID NO: 288)
                                 : EQQPELKPGKGTPGQEKKGKSSTSES*
      75 A30502
                                 : EQQPELRPGKGTPGQEKKGKSSTSES*
      76 MUSIGHAAG
                                                                    (SEQ ID NO: 289)
                                 : POOPELKPGKGTPGOEKKGKSSASES*
      77
         B30502
                                                                    (SEQ ID NO: 290)
                                 : EQQPELKPGKGTPGKQKKGKSSTSZS+
25
      78
         MUSIGHADG
                                                                    (SEQ ID NO: 291)
                                 : EQOPELKPGKGTHGKOKKGKSSTSES*
      79 MUSIGHTV
                                                                    (SEQ ID NO: 292)
                                 : EQQPELKPGKGSHGKQKKGKSSTSES*
      80 MUSIGHAANA
                                                                    (SEQ ID NO: 293)
                                                                    (SEQ ID NO: 294)
(SEQ ID NO: 295)
      81 MUSIGHZR
                                 : EQQPELXPGKGSBGKQKKGKSSASES*
                                 : ZQQPELKPCKCTHCKQKXCKSSTFZS*
      82 MUSIGHAI
      83 MUSICHALA
                                 : POOPELXPGKGTHGKOKOGKSSTFES*
                                                                    (SEQ ID NO: 296)
30
                                 : ECOPELEPGEGTHGKERKDESSTSES*
                                                                    (SEQ ID NO: 297)
      14
         PL0011
                                 : BOOARLKPGKGSHGKOKKGKSSTSES+
                                                                    (SEQ ID NO: 298)
      45 MUSICKCLS
                                 : EQQPELXPGKGTHGKQKKSNSSTSES+
                                                                    (SEQ ID NO: 299)
      86 MUSICHADY
                                 : OCCARLEPGEGAPGOZUCGESTSZS*
                                                                    (SEQ ID NO: 300)
      87 MUSIGEWYX
                                 : QQQAELRPGKGAPGQEKKGKSSTSDS+
                                                                    (SEQ ID NO: 301)
      88 MUSIGRADO
      89 MUSIGHVEM
                                 :OOGAELRPGKGVPGQEKKGKSSTSDS+
                                                                    (SEQ ID NO: 302)
(SEQ ID NO: 303)
35
                                 : COOPELKPGRGAPGKGKKGKSSTSES*
      90 A24672
                                 : OCOPELEPCEGAPCEGERENCESTSES*
                                                                    (SEQ ID NO: 304)
      91 NUSIGHJG
                                 * EQQPEAKPGKGTHGKQKXGKSSTSDS*
                                                                    (SEQ ID NO: 305)
      92 JL0044
                                 : QQQAELIPGKGTHGKEKKDKSSTSDS*
                                                                    (SEQ ID NO: 306)
      93 MUSIGHBA
                                 : QQQAXLRPGKGAPGQGKKGKSSTSES*
                                                                    (SEQ ID NO: 307)
      94 MUSICHAGE
                                                                    (SEQ ID NO: 308)
                                 : QQQAELKPGRGTPGQEKKGKSSTSES*
      95 MUSICHVBK
                                 : EQQAELRAGKGTPGQEKKGKSSTSES*
                                                                    (SEQ ID NO: 309)
      96
         A36194
                                                                    (SEQ ID NO: 310)
(SEQ ID NO: 311)
                                 : EQQAELRPCKGTPGQZKKGTSSTSES*
      97
         MUSICHVEJ
                                 : QQQAKLRPGKGTPGHEKKGTSSTSES*
      98
         MUSICHADY
                                                                    (SEQ ID NO: 312)
                                 : QQQAELXPGKGTPGHZKKGTSSTSES*
      99
         MUSICHAAT
                                 : QQQAZIRPGKGTPGHENKGTSSTSES*
                                                                    (SEQ ID NO: 313)
     100 MUSICHJL
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(SEQ ID NO: 314)
(SEQ ID NO: 315)
(SEQ ID NO: 316)
(SEQ ID NO: 317)
                                   :QQQAEVRPGKGTPGHEKKGTSSTSES*
       101 MUSIGHABM
       102 MUSIGHFU
                                   : QQQAELKPGKGTPGHENKGTSSTSES*
                                   : QQQAELRPGKGTPGQQKKGKSSASES*
       103 MUSIGHZZB
5
       104 HV06SMOUSE
                                   : HQQAELXPGKGTPGQQKKGKSSTSES*
                                                                        (SEQ ID NO: 318)
       105 MUSIGHRD
                                   : EQQVELRAGKGTPGQEXXGKSSTSES*
                                                                        (SEQ ID NO: 319)
                                   : EQQAELRPGKGTPGQEKQGTSSTSES*
       106 MUSIGHVBH
                                                                        (SEQ ID NO: 320)
                                   : EQQAELRPGKGTPGHDNKGTSSTSES*
       107 HV01$HOUSE
                                                                        (SEQ ID NO: 321)
(SEQ ID NO: 322)
                                   :QQQAEVRPGKGTPGHEKKGRSSTSES*
       108 MUSIGHADN
                                   :QQQAELRPGKGTPGQQKKDKSSTSES*
       109 HVOSSHOUSE
10
                                                                        (SEQ ID NO: 323)
       110 MUSIGHAEF
                                   : QQQAELKPGKGTPGQQKKDKSSTSES*
                                                                        (SEQ ID NO: 324)
                                    : QQQAELKPGKGTPGQQKKDKSSTSDS*
       111 MUSIGHAAN
                                                                        (SEQ ID NO: 325)
(SEQ ID NO: 326)
(SEQ ID NO: 327)
                                    : QQQAELKPGKGSPGQQKKDKSSTSES*
       112 MUSIGHAAB
                                    : QHQAELKPGKGTPGQQKXXXSSTSES*
       113 C30560
                                    : QQQAELXPGKGTPGQQNXDKSSTSES*
       114 PS0024
                                                                        (SEQ ID NO: 328)
(SEQ ID NO: 329)
                                    : EQQAELRAGKGIPGQEXKGKSSTSES*
15
       115 MUSIGHRG
       116 MUSIGHAAB
                                    : QQQAELRPGKGTPGQEKKSKSSTSES*
                                                                        (SEQ ID NO: 330)
(SEQ ID NO: 331)
                                    : QQQSELKPGKGTPGQEKKSKSSTSES*
       117 MUSIGHLX
                                    : QQQTELXPGRGTPGQEXXSKSSTSES*
       118 HV045MOUSE
                                    : EQQAELRTGKGTPGQERKGKSSTSES*
                                                                        (SEQ ID NO: 332)
     . 119 MUSIGHVBG
                                                                        (SEQ ID NO: 333)
                                    : OCCAPLKPGKGTPGQQKKDKSSTPES*
       120 MUSIGHOX
                                                                        (SEQ ID NO: 334)
(SEQ ID NO: 335)
                                    : EQQAELRPGTGAPGQEKKGKSSTSES*
20
       121 MUSICHAAR
                                    : QQQPEVRPGKGTHAKQKKGKSSTSES*
       122 HV15SHOUSE
                                    : QQQPEVRPGKDTHAKQKKGKSSTSES*
                                                                        (SEQ ID NO: 336)
       123 MUSIGHAAU
                                    :QQQAELKPGKGTPEQEKKGKSSTSES*
                                                                        (SEQ ID NO: 337)
       124 MUSIGHVBO
                                   : EQQTELRAGKGTPGQEKKGRSSTSZA*
                                                                         (SEQ ID NO: 338)
        125 A26405.
                                   : QQQAZLKPGKGTPGREKKSKPSTSZS*
                                                                         (SEQ ID NO: 339)
       126 HV10SMOUSE
                                    : QQQSELLOGKGTPGREKKSKPSTSES*
                                                                         (SEQ ID NO: 340)
        127 MUSIG3B44
                                                                        (SEQ ID NO: 341)
(SEQ ID NO: 342)
(SEQ ID NO: 343)
                                    : QQRAELKPGKDTPGREKKNKPSTSES*
        128 MUSIG3B62
                                    : QQQAELEPGKGTPGREKKSTSSTSES*
        129 HV09$MOUSE
                                    : QQQAELKPGKGTPGQEKKSTSSTSDS*
        130 MUSIGKCLP
                                                                         (SEQ ID NO: 344)
                                    : QQQAELPPGKGTPIQQKXDKSSTSES*
        131 MUSICBE
                                                                         (SEQ ID NO: 345)
                                    : QQQAEFKPGKGTPGREHRSKPSTSES*
       132 HV11$MOUSE
                                    : QQQAELRPGKGALGQEKKGKSSTSDS*
                                                                         (SEQ ID NO:
30
                                                                                      346)
        133 MUSIGHMC
                                                                         (SEQ ID NO: 347)
                                    : QQQPEVKPGKGAPGKGNTDKSSTSES*
       134 MUSIGHAGW
                                                                         (SEQ ID NO: 348)
(SEQ ID NO: 349)
(SEQ ID NO: 350)
                                    : EQQAEVRAGEGSPGQEEEGESTSES*
        135 MUSIGER
                                    :QCLAELEPGKGTPGHEKKGISSTSES*
        136 MUSICHVAD
                                    : QQQAELEPGKGEPEQEKKGTSSTSES*
        137 MUSIGHVAF
                                                                         (SEQ ID NO: 351)
                                    :QQQPELEPGEGRIGKENEGESTSES*
        138 PL0012
35
                                    : QQQTELPPGRGTTGQERKGKSSTSES*
                                                                         (SEQ ID NO: 352)
        139 MUSIGGVD2 ...
                                                                         (SEQ ID NO: 353)
                                    : OHOAELXPGKGTPGHENKVTSSTSES*
        140 906824
                                                                         (SEQ ID NO: 354)
                                    : EQQAELRACKGTPGQEQKAKSSTSES*
      · 141 MUSIGHTS
                                     : QQQAELKPGKGTPGQQKTGTSSTTES*
                                                                         (SEQ ID NO: 355)
        142 MUSIGHALE
                                     : QQQAELEPGKGNPGQEKKSTSSASES*
                                                                         (SEQ ID NO: 356)
        143 MUSIGHES
                                                                         (SEQ ID NO: 357)
                                    : EQQTVLRPGKGTFGQQKKGTSATHES*
        144 MUSIGHAXA
                                                                         (SEQ ID NO: 358)
40
                                     : QOLTELEPGNGTPGQEERSKSSTSES*
        145 HV50$MOUSE
                                                                         (SEQ ID NO: 359)
                                     : QQQSVLPPGKGTPGQEKGTSSTSKS*
        146 MUSIGHVBP
                                     : LQQPVLKPGKGSHGKQKXXXSTSES*
                                                                         (SEQ ID NO: 360)
        147 PH0100
                                     : EQQPETKPGKGTLGKQKKSKSSTSES*
                                                                         (SEQ ID NO: 361)
        148 MUSIGHAYA
                                                                         (SEQ ID NO: 362
(SEQ ID NO: 363
                                    : QQQAELKPGQGTPGQEKKNKSSTPEF+
        149 MUSIGHCP2 .
                                     : EQQAELEPGEGEPEOPEOGTSSTSET*
```

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150 MUSIGHDZ

```
: Eqqaelrpgkgnpeqpkqgtsttset•
        151 MUSIGHNPI
                                                                              (SEQ ID NO: 364)
                                    : EQQAELKPGKGNPEQPKQGTSSTSET+
: EQQAELKPGKGNPEQPKQDTSSTSET+
        152 506823
                                                                             (SEQ ID NO: 365)
                                                                              (SEQ ID NO: 366)
        153 MUSIGHASA
                                                                              (SEQ ID NO: 367)
(SEQ ID NO: 368)
                                       : EQQAELKPGKGNPEQPKQGTSSTSGT*
        154 503484
5
                                    : EQQAEVKPGKGNPEQPKQGTSSTSET*
: EQQAELRPGKGNPEQPKQVTSSTSET*
: EQQAELRPGKGNPEQPKQITSSTSET*
: EQQAELRPGRGNPEQPKQVTSSTSET*
: EQQAELRPGRGNPEQPKYVTSSTSET*
                                      : EQQAEVKPGKGNPEQPKQGTSSTSET*
        155 MUSIGHVAA
                                                                              (SEQ ID NO: 369)
        156 MUSIGHNPD
        157 MUSIGHNPB
                                                                              (SEQ ID NO: 370)
                                                                              (SEQ ID NO: 371)
(SEQ ID NO: 372)
        158 MUSIGHEC
                                       : EQQAELRPGRGNPEQPXHVTSSTSET*
        159 MUSIGHNPC
                                       : EQQAELRPGKGNTEQPKQVTSSTSET*
        160 MUSICHNPP
                                                                              (SEQ ID NO: 373)
10
                                       : EQQAELKPGKGNTEQPKLITSSTSET*
                                                                              (SEQ ID NO: 374)
(SEQ ID NO: 375)
(SEQ ID NO: 376)
      161 MUSIGHNPE
                                       :TGQAELRPGKGAPEQGKKGKSSTSDR*
        162 A27635
                                      :QYQAELRPGKGTPRQQKKGKSSTSES*
        163 MUSICHXW
                                      : QQQAVLRHGKGTHGQEKKGKSSTSES*
        164 MUSIGHIZA
                                                                               (SEQ ID NO: 377)
                                       : OOOTKLEPGRGTPGQGRKGKSSTSGS+
                                                                               (SEQ ID NO: 378)
(SEQ ID NO: 379)
       . J5 MUSIGHEN
                                       : EQQAELRAGKGTPGQEKKGKSSVYFA*
        166 MUSIGHRH
                                      : EQQAELKAGKGTPGQQKQGESTRSET+
        167 HV00SHOUSE
                                                                               (SEQ ID NO: 380)
                                      : QQKAELAASKGTPGQEKKGRSSTSES*
: QQQTELRPGKGTPGQEKRGKSSHLRL*
        168 NS1719H
                                                                               (SEQ ID NO: 381)
                                                                              (SEQ ID NO: 382)
(SEQ ID NO: 383)
        169 MUSIGHZAD
                                    : EXVGGLQGSSFDPGKASKGTSQRAET.
        170 B30515
                                     : eqqadlklgkgnpeqpklatpstset+
: eqvgglkpgkgtpdksdvkdnakset+
: dqqpdlkpssgspghpskstskttet+
                                                                               (SEQ ID NO: 384)
(SEQ ID NO: 385)
(SEQ ID NO: 386)
        171 MUSIGHEB
        172 E27889
20
        173 MUSIGHAAC
                                     : DOOPDLKPSSGSPGNPSKSTSKTTET+
        174 HV61$MOUSE
                                                                               (SEQ ID NO: 387)
        175 MUSIGVHR2
                                      : DOOPDLKPSSGSPGNPSKSTSKTAET*
: DOOPGLKPSSGSPGNPSKSTSKTTET*
                                                                               (SEQ ID NO: 388)
(SEQ ID NO: 389)
(SEQ ID NO: 390)
        176 PL0100
                                     : DOOPGLKPSSGSPGNPSKNTSKTTET*
        177 MUSIGHAAO
                                     : DQQPGLKPSSGSPGDPSKTTSKTTET*
: DQQPGLKPSSGSPGNPSKTTSKTTET*
        178 MUSIGHGA6
                                                                               (SEQ ID NO: 391)
                                                                               (SEQ ID NO: 392)
(SEQ ID NO: 393)
        179 MUSIGHJY
                                      : DHQPGLKPSSGSPGNPSKNTSKTTET*
        180 MUSIGHGAL
                                                                               (SEQ ID NO: 394)
(SEQ ID NO: 395)
(SEQ ID NO: 396)
                                       : DOOPGLEPSSSPGNPSRSTSKTTET+
        181 MUSIGHXX
                                       : DOOPGLEPSAGSPGNPSKSTSKTAET*
        182 HV62$MOUSE
                                       : POOPGLEPSSGSPGNPSESTSETS
        183 MUSIGHAAGA
                                        : DQQPGLKPSSGSPGNPSKNTSKTIET+
        .84 MUSIGHGAS
                                                                               (SEQ ID NO: 397)
                                        : DOOPGLEPSSSPGDPSKMTSKTPET+
                                                                               (SEQ ID NO: 398)
30
        185 MUSIGHGA4
                                                                               (SEQ ID NO: 399)
                                        : BOOPSLAPSSGSPGNPSKSTSATTET*
        186 MUSIGHAGI
                                        : DQQPGLXPSSGSPGNPSKNTSETTET*
                                                                               (SEQ ID NO: 400)
        187 PL0102
                                                                               (SEQ ID NO: 401)
(SEQ ID NO: 402)
        188 HV46$HOUSE
                                        : DOOPGLEPSSGSPGNPSKHTSETTZT+
                                        : ZOOPSLKPSSGSPGNPSKSTSKTSET*
        189 MUSICHZT
                                        : EQOPSLICPSSGSPGNPSKSTSRTTET*
                                                                               (SEQ ID NO: 403)
        190 MUSIGHAGD
                                        : EQQPSLIPSSGSPGNPSKSTSKTAET+
35
                                                                               (SEQ ID NO: 404)
        191 MUSIGHAGO-
                                        : DOOPDLEPSSGFPGMPSKSTSKTTET*
                                                                               (SEQ ID NO: 405)
        192 NUSIGANJZ
                                        : DOOPSLKPSSGSPGKPSKSTSKTNET*
                                                                               (SEQ ID NO: 406)
        193 MUSIGHAFX
                                        : ZQQPSLKPSSGSPGNPSKSTFKTSET*
                                                                               (SEQ ID NO: 407)
        194 MUSIGRAGE
                                        : EQQPSLKPSSGSPGNPSKSTSTTSET*
                                                                               (SEQ ID NO: 408)
        195 MUSIGRAGE
                                        : EQQLILKPSSGSPGNPSKSTSKTTET*
                                                                               (SEQ ID NO: 409)
        196 MUSIGHAGE
                                        : QQQPGLKPSPGPPGKPSQSTSKTTET*
                                                                               (SEQ ID NO: 410)
40
        197 MUSIGHAAN
                                        :QQRPGLAPSSGSPGRSTRSHSKQTDT+
        198 HV43SMOUSE
                                                                               (SEQ ID NO: 411)
                                        : CORPGLAPSGSPGKSAKSNSKOTOT*
                                                                               (SEQ ID NO: 412)
(SEQ ID NO: 413)
        199 MUSICHUVI
                                        : CORPGLAPSGSPGKSAMSNSKQTOT*
        200 MUSIGHAZI
                                        *CORPGLAPSSGSPGKSAISHSKOTDT*
                                                                               (SEQ ID NO: 414)
        201 MUSIGHBP
                                        :QQKPGLQPSSGSPGKAAISHSKQSHT*
                                                                               (SEQ ID NO: 415)
        202 MUSIGHZZA
                                       :QQXPGLQPSSGSPGXAAISNSXQAMT*
                                                                              (SEQ ID NO: 416)
(SEQ ID NO: 417)
45
        203 MUSIGMUV2
                                      *TOIDAENTARESESESES PERSANSHEROIDT
        204 A32456
                                  :QQKPSLQPSSDSPGKAAMSHSKQADT*
                                                                               (SEQ ID NO: 418)
        205 MUSIGHMS
```

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HUMAN HEAVY CHAIN SURFACE PATCHES

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```
: ERVGDLEPGRGIPGKAPKGDSKKIET•
                                                                     (SEQ ID NO: 419)
           1 HUMIGHVS
                                                                     (SEQ ID NO: 420)
                                   : ERVGDLEPERGIPGKAPKGDSKKIET*
           2 HUMIGHVR
                                                                     (SEQ ID NO: 421)
                                   : EQVGGLKPGRGTPGKAPKGDSKKTET*
           3 H36005
                                                                     (SEQ ID NO: 422)
                                   : EQVGGLQPGKGTSGKASKGDSKKTET*
           4 PL0122
                                                                     (SEQ ID NO: 423)
                                   : EQLGGLQPGRGTPGKBSKGDSKRAET*
           5 HV3D$HUMAN
                                                                     (SEQ ID NO: 424)
                                   : EQLGGLQPGRGTPGKDSKGNSKRAET*
           6 HUMIGHAT
                                                                     (SEQ ID NO: 425)
                                   : EQLGGLOPGRGTPGKDSRGNSKRAET*
           7 B34964
                                                                     (SEQ ID NO: 426)
                                   : EQVGGLQPGRGTPGKDSKGHSKRAET*
           8 A34964
                                                                     (SEQ ID NO: 427)
10
           9 PL0123
                                   : EQVGGLQPGRGTPGKDSKGNAKRAET*
                                                                     (SEQ ID NO: 428)
          10 HVJPSHUMAN
                                 : EQVGGLQPGRGTPGKDSKGDSRRAET*
                                   : EQVGGLQPGRGTPGKDSKGNSRRAET*
                                                                     (SEQ ID NO: 429)
          11 JL0048
                                                                     (SEQ ID NO: 430)
                                   : OOVGGLEPGRGTPGKDSKGBSKRAET.
          12 HV3BSHUMAN
                                                                     (SEQ ID NO: 431)
          13 HUMIGHBV
                                   : EQLGDLQPGRGTPGKASKGNSKRAET+
                                   : equgglqpgrgttgkdskgdskraet*
                                                                     (SEQ ID NO: 432)
          14 HV3ESHUMAN
                                   : QQVGGVQPGRGTPGRDSKGHSKRAET*
                                                                     (SEQ ID NO: 433)
15
          15 PL0116
                                   : QQVGGVQPGRGIPGKDSKGNSKRPET*
                                                                     (SEQ ID NO: 434)
          16 HV3K$HUMAN
                                   : EQVGGVQPGRGIPGKDSKGDSKRPET*
                                                                     (SEQ ID NO: 435)
          17 NS2PB4H
                                   : QQVGGVQPGRGTPGKDSKGDSKRPET+
                                                                     (SEQ ID NO: 436)
          18 HV3I$HUMAN
                                   : QKVGGVQPGRGTPGKDSKGNSKRTET*
                                                                     (SEQ ID NO: 437)
          19 HV3J$HUMAN
                                                                     (SEQ ID NO: 438)
                                   : QEVGGVZPGRGTPGRBSKGBSKRAET*
          20 HV3GSHUMAN
                                                                     (SEQ ID NO: 439)
                                   : POLGGLOPGRGTPGROSHGDSKQAZT*
          21 HV3H$HUMAN
20
                                                                     (SEQ ID NO: 440)
                                   : eqlgglqpgrgspgkdthgdskel2t+
          22 HV3OSHUMAN
                                   : AQLGGLOPGRGTPGKDSHGDSKQAZS*
                                                                                  441)
                                                                     (SEQ ID NO:
          23 HV3N$HUMAN
                                   : EQLGGLQPGRGTPGKVSQGDSKQAZT*
                                                                     (SEQ ID NO:
                                                                                  442)
          24 HVJRSHUMAN
                                                                     (SEQ ID NO: 443)
                                   : POVGGLOPGRGTPGKVSQGDSKEPIT*
          25 HV3P$HUMAN
                                   : EQLGGLQPERGTPGKESKGNSNRAET*
                                                                     (SEQ ID NO: 444)
          26 HUNIGHCV
                                                                     (SEQ ID NO: 445)
                                   : PQVGDLQPGRGBPGKDSKGNAKRVET*
          27 HV3TSHUKAN
25
                                   : EQVGDLQPGRGNPGKDSKGNAQRPET+
                                                                     (SEQ ID NO: 446)
          28 HVJUSHUMAN
                                   : QQVGGVQPGRGTLGKDSKGNSKRAET+
                                                                     (SEQ ID NO: 447)
          29 PL0098
                                                                     (SEQ ID NO: 448)
                                   :QZVGGAZPGRGSPGKASKGBSKRAET+
          30 HVJHSHUMAN
                                   : QQVGGLKPGRGSPGKDSKGNAORTZT*
                                                                     (SEQ ID NO:
                                                                                  449)
          11 HV3A$HUKAN
                                   : DQVGGLKPGRGTPGKHSHGDSKTPET*
                                                                     (SEQ ID NO: 450)
          32 HV3SSHUMAN
                                                                     (SEQ ID NO: 451)
                                   : COLGGLOPGRGTSREDSKGNSKRAET*
30
          33 HUNIGHAW
                                                                     (SEQ ID NO: 452)
                                   : EQVGALQPGRGTPGKDSQADSKEAZT*
          34 HV3QSHUMAE
                                                                      (SEQ ID NO: 453)
                                   : EOLGGLOPGRGTPGK----VEGSVET*
        . 35 A36040
                                   : EQVGAFQPGRGMSGKASKGDSKRPDT.
                                                                     (SEQ ID NO: 454)
          36 HUNIGHAM
                                   : EQVGAFQPGKGNSGKASKGDSKRPDT*
                                                                      (SEQ ID NO: 455)
          37 HUMIGHAO
                                                                      (SEQ ID NO: 456)
                                   : DOVGAPOPGKGHSGKASKGDSHRPDT*
          38 HUNIGHAR
                                   : QQVGGVQAGRAMPGKDSRGISKRTET*
                                                                      (SEQ ID NO: 457)
          39 HV3LSHUMAN
35
                                                                      (SEQ ID NO: 458)
                                   : QQVAEVKPGKGTPGQQKQGESTRSET*
          40 HVLASHUKAN
                                                                      (SEQ ID NO: 459)
                                    :QQVAEVRPGKGTPGQQKQGTSTRSET*
          41 A32483
                                                                      (SEQ ID NO: 460)
                                    : QQVAEVKPGKGTPGQQKQGTSARSET*
          42 HUNIGHAY
                                   :QQVAEVEPGKGTPGQQKQGTSIRSDT*
                                                                      (SEQ ID NO: 461)
          43 HUNIGHCU
                                    : QQVAEVKPGRGTPGQEKQGTSIRSDT*
                                                                      (SEQ ID NO: 462)
          44 HUNIGHBS
                                    : QQVAEVRPGKGTPGQQKQGTSTRSDT*
                                                                      (SEQ ID NO: 463)
40
          45 HUMIGVHLS
                                                                      (SEQ ID NO: 464)
                                    : QQVGEVKPGRGTPGQQXQDTSTRSDT*
          46 HUMIGHBX
                                                                      (SEQ ID NO: 465)
                                    :QQVAEVKPGRGTPGHPRQGASTRSDS*
          47 HV1CSHUMAN
                                                                      (SEQ ID NO: 466)
                                    : QQVSELKPGKGTPGQQGTGTSVKAET*
          48 H34964
                                                                      (SEQ ID NO: 467)
                                    : ZQVAEVKPGKGSPGKPSQGKSIKAST*
          49 HUMIGHCY
                                                                      (SEQ ID NO: 468)
                                    : EQVAEVKPGRGSPGKPSQGKSIKAST*
          50 PL0119
```

			• •				
	51	HV1F5HUMAN	:QQVAEVKPGRGDPGRPRQASSTISAT*	(SEQ	ID	NO:	469)
	52	D34964	: eqvaevpqgkgrpgkslqgkslkast+	(SEQ	ID	NO:	4701
	53		: QQMAEVKPGRGTPGKPGVVPSPPSET+	(SEQ			471)
		HV1ESHUMAN	: QQVAEVKPGRGTPGRYIWEPSFFNEG+	(SEQ			472)
5			: OOQAGLKPSSGSPGKPSKSTSKTAAT+				•
5	55	JL0047		(SEQ			473)
	56	HUMIGHBW	:QQQPGLKPSSGSPGKPSKSTSKTAAT+	(SEQ	ID	NO:	474)
	57	E34964	:QQQPGLKPSSGSPGKPSKSTSHTAAT*	(SEQ	ID	NO:	475)
	58	HUNIGHCW	:QQQPGLKPSSGSAGKPSKSTSKTAAT*	(SEQ			476)
	59	HV2F\$HUMAN	:rqqpglkpssgppgkpsrgtsrsaat+	(SEQ	ID	NO:	4773
	. 60	HV2ISHUMAN	:QQQAGLKPSSGSPGRTSKSTSKTAAT+	(SEQ	ID	NO:	478)
10	61	HV2G\$HUMAN	: QQEPGLRPSSGTPGRTPRSTSKTAAT*	(SEQ			479)
	62	HEATCRM	: xqepglrpssgspgrtprstsktaat+	(SEQ	ID	NO:	480)
	63	PS0091	: QQQPGLKPSSGSPSRVSKSTSKTPET*	(SEQ	ID	NO:	481)
	64	HUMIGHDA	: QHQAGLKRSSGPPGKPSTSTSKTAAT*	SEQ		NO:	482)
	65	A26555	: Zqesglxptsgspgkpsksrskaada•	SEQ	TD	NO:	483)
	66	HV2ESHUMAN	: otkptlkpttgspgrpskstskdpvt+	SEQ	ĪD		484)
15	67	HV2DSHUMAN	: QTKPTLKPTTGSPGKPSRSTSRDPV9*	(SEQ		NO:	485)
	68	A36005	: etrpalkpttgspgktskttskdpvt*	(SEQ		NO:	486)
	69	HV2HSHUMAN	: Onrpalkattgspgktsettskopat*				
		HV2ASHUMAN	:OTTPALKPKTGSPGKTSRTDSKNPVT+	(SEQ		NO:	487)
	70			(SEQ		NO:	488)
	71	HV2C\$HUNAN	: QTRPALRPTTGSPGEASETTSKGPGT+	(SEQ	ID	NO:	489)
	72	HV28\$HUNAN	: QTRPALKPTTGSPGKTSETTSRDTAY*	(SEQ	ID	NO:	490)
20	73	JL0049	: Legyqlwggrgisrkyarghgkrdes+	(SEQ		NO:	
20				/			· · · /

EXAMPLE 2

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DETAILED DESCRIPTION OF METHOD FOR CONSTRUCTING THREE-DIMENSIONAL MODEL OF ANTIBODY VARIABLE REGION

[0070] The references cited in the text below are listed at the end of this Example.

[0071] The first antibody Fab structure was determined in 1972. Since then, no more than about twelve Fab structures have been published, a number that represents a very small fraction of the total antibody repertoire (>10⁸ antibodies). To understand the molecular basis of this antibody diversity will require knowledge of either a large number of x-ray structures, or the rules by which combining site topography is governed. The development of such prediction rules has now reached the point where variable regions of antibodies can be modelled to an accuracy approaching that of the medium resolution x-ray structure.

[0072] The interaction of an antibody with its cognate antigen is one of the most widely accepted paradigms of molecular recognition. To understand the antibody-antigen interaction in atomic detail requires knowledge of the three-dimensional structure of antibodies and of their antigen complexes. Traditionally such information has come from x-ray crystallographic studies (see Davies et al., for review (Davies et al., 1988)).

[0073] The modelling of antibody combining sites was first attempted by Padlan & Davies (Padlan et al., 1976) at a time when very few antibody structures were known. Nonetheless, Padlan and colleagues recognized that the key lay in high structural homology that existed within the β-sheet framework regions of different antibody variable domains. The antigen combining site is formed by the juxtaposition of six interstrand loops, or CDRs (Complementarity Determining Regions) (Kabat et al., 1987), on this framework. If the framework could be modelled by homology then it might be possible to model the CDRs in the same way. Padlan and Davies (Padlan et al., 1976) reasoned that CDR length was the important determinant of backbone conformation though the number of antibody structures was insufficient to thoroughly test this maximum overlap procedure (MOP). This notion was not picked up again until the early 1980's when Pedersen and Rees proposed a similar approach to modelling antibody combining sites based on a more extensive analysis of antibody structures (de la Pas et al., 1986).

[0074] Those essentially knowledge-based procedures are best exemplified for antibodies by the work of Chothia & Lesk (Chothia et al., 1986) who, in 1986, extended and modified the MOP procedure by introducing the concept of "key" residues. These residues allow the further subdivision of CDRs of the same length into "canonical" structures which differ in having residues at specified positions that, through packing, hydrogen bonding or the ability to assume unusual values of the torsion angels φ, ψ and ω, determine the precise CDR conformation (Chothia et al., 1989). Similar knowledge-based methods have been proposed for predicting loop conformations in general (Thornton et al., 1988; Tramontano et al., 1989). These methods rely on the crystallographic database of protein structures. However, none of the above knowledge-based methods has been totally successful. In particular, the MOP or canonical structure approaches have succeeded in modelling only five of the six CDRs. This stems from the fact that the third CDR of the

heavy chain, H3, is more variable in sequence, length and structure than any of the other CDRs.

[0075] To deal with this problem several groups have attempted to use ab initio methods to model the combining site (Bruccoleri and Karplus, 1987). The requirement with such methods is that the total allowable conformational space accessible to a particular CDR is sampled. Typical of purely geometric approaches is that of Go & Sheraga (Go and Sheraga, 1970) and more recently Palmer & Sheraga (Palmer and Sheraga, 1991), where the problem is reduced to one in which the central region of the polypeptide backbone, having characteristic bond length and bond angles, is constructed between the end points of the loop (CDR if an antibody loop) by a "chain closure" algorithm. In a modification of this algorithm, Bruccoleri & Karplus (Bruccoleri and Karplus, 1987) introduced an energy minimization procedure which greatly expanded the domain of conformational space searched during the chain closure procedure. This modification is incorporated into the conformational search program CONGEN (Bruccoleri and Karplus, 1987), which also allows the user to choose any set of standard bond length and bond angels such as the CHARMM (Brooks et al., 1983) standard geometry parameter sets. Other approaches such as minimization (Moult and James, 1986), or molecular dynamics (Fine et al., 1986) either fail to saturate conformational space or are unable to deal with the problem of long CDRs. Whichever of the ab initio methods is employed however, the problem is one of defining the selection criteria in such a way as to allow the unambiguous identification of the correct structure (in this context correct is defined by reference to an appropriate X-ray structure) within the ensemble of candidates, for every CDR. To date this has not been possible.

[0076] Recently a more holistic approach has been taken to the modelling of CDRs which combines the advantages of knowledge-based and *ab initio* methods in a single algorithm known as CAMAL (Combined Algorithm for Modelling Antibody Loops) (Martin et al., 1989; Martin et al., 1991). Previously this algorithm has been used to model individual CDRs in the presence of the crystal structure conformations of the other five. As is demonstrated below, CAMAL is able to predict the backbone conformations of all six CDRs of the antibody combining site to an accuracy approaching that of medium resolution x-ray structures. In addition the algorithm includes a procedure for selecting and fitting together the light and heavy chain framework regions prior to generation of CDR conformations, thus making possible the prediction of the entire variable region. Furthermore a new Monte Carlo (MC) simulated annealing method has been developed for the determination of sidechain conformations.

The Framework Region

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- [0077] Antibody framework regions consist of conserved β-strands that form the β-barrel structure characteristic of immunoglobulin V-type regions. In the procedure described here each V-region is built from a database of known antibody structures, using sequence homology for selection of the light (L) and heavy (H) chain V-domains. The two domains are then paired by least squares fitting on the most conserved strands of the antibody β-barrel (Table 2 and Figures 5 & 6). The strand orientations were determined by analyzing the barrels of known antibody crystal structures.
- Eight antibodies were analyzed using a multiple structure fitting program as follows. Seven structures were fitted onto one of the set selected at random and mean coordinates were calculated. All eight structures were then fitted onto these mean coordinates and new mean coordinates determined. This procedure was iterated until the mean coordinate set converged (5-10 cycles). The variance for the mean coordinates at each barrel point (N,Cα,C) was calculated. In Figure 5 this variance is plotted against the projected positions of these points onto the conjugate axis of the barrel.
 - [0078] Strand 8 and all but two residues of strand 7 in both light and heavy chains were eliminated as they showed deviations greater than 3σ (standard deviation units) from the mean coordinates. These two strands comprised the takeoff points of CDR H3, and suggests that any knowledge-based prediction of CDR H3 would have to account not only for sequence and length variation in the CDR itself, but also for the position of the participating strands. The remaining mean coordinates were used as a scaffold onto which the L and H chains were fitted. Strands 7 and 8 in the final framework were obtained from the database structure used in the construction. The framework strands are marked + in the multialignment in Table 2.
 - [0079] The sidechains were then replaced using a 'maximum overlap' method, in which sidechain templates were fitted on backbone atoms with the sidechain torsion angles being adjusted to match those of equivalent torsions in the parent sidechain.

The Combining Site

- [0080] The procedure for predicting the structure of combining sites combines a database search with a conformational search procedure. The architecture of the program suite to perform this task is outlined in Figure 7.
- [0081] The database search utilizes distance constraints for each of the six CDR loops determined from known antibody structures. These constraints were determined by calculating $C\alpha$ - $C\alpha$ distances within known loops and using a search range of \underline{x} + 3.5 σ (the mean \pm 3.5 standard deviation units). A database containing all the proteins in the Brookhaven Protein Databank (Bernstein et al., 1977) is then searched for fragments which satisfy the constraints for

a loop of the required length. The middle section of the loop is then deleted and reconstructed using the conformational search program CONGEN (Bruccoleri and Karplus, 1987). For loops of six or seven residues, the structure database appears to saturate the conformational space available to the backbone adequately and only sidechains are built by conformational search. Loops shorter than six residues are built by conformational search alone since this is computationally feasible and the number of loops selected from the database becomes unacceptably large as loop length decreases.

[0082] When modelling a complete combining site, loops of 6 or more residues are modelled individually with the other loops absent. If the loops are built consecutively, small errors can accumulate leading to a poor result (Martin, 1990). All the loop conformations are then evaluated using a solvent modified potential, which excludes the attractive van der Waals and electrostatic terms of the non-bonded energy function contained within the GROMOS (Aqvist et al., 1985) potential. The lowest five energy conformations are selected and filtered using a "structurally determining residue" algorithm (FILTER), based on backbone torsion angles observed in the original database loops. Since the database search is not used for the shortest loops of 5 residues or fewer, the FILTER algorithm cannot be used. Energy is thus the only available selection criterion and the short loops are built last, in the presence of the longer loops.

Side Chains

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[0083] The determination of sidechain positions was previously done using the iterative sidechain determination algorithm described by Bruccoleri et al. (Bruccoleri and Karplus, 1987). Unfortunately the CHARMM (Brooks et al., 1983) force field fails to select the correct conformations of exposed hydrophobic sidechains. There is no penalty for having an exposed uncharged atom, without solvent present. CONGEN is also unable to saturate the conformational space for a large number of sidechains (more than 6 residues).

[0084] Recently Lee et al. (Lee and Levitt, 1991; Lee and Subbiah, 1991) has proposed a method for searching conformational space for a large number of sidechains using MC simulated annealing. A simple energy function is used for the evaluation of conformations generated by a biased random walk:

$$E = \sum_{i=1}^{n} \epsilon_{o} ((\frac{r_{o}}{r})^{6} - 2(\frac{r_{o}}{r})^{12}) + \kappa_{o} \cdot COS(3\omega)$$

Where the first term is a simple Lennard-Jones potential which evaluates the non-bonded contacts between the atoms in a given molecule, the second term is a simple torsional term which only applies to C-C bonds. The torsional term biases the function towards 60° rotamers. ϵ_0 and κ_0 are constants. The metropolis function:

$$P = C^{\frac{-\delta E}{T}}$$

is used to evaluate the energy function. Any move which results in a decrease in energy is accepted, and any move which results in a positive δE is only accepted with the probability P. This simple method can be used to search the large conformational space defined by a set of torsion angles in amino-acid sidechains, and find or define the global minimum which exist for a set of sidechains. T is the simulation temperature.

[0085] When searching sidechain conformations using this method the simulation system usually gets trapped in an energetic minima well before the global minimum is encountered, at a high temperature, without the solution space having been searched sufficiently. This problem can be solved by truncating the *Lennard-Jones* potential, thus allowing atoms to pass through each other. In reality this function would converge towards infinity when the distance *r* between the atoms approaches zero.

[0086] The evaluation of sidechain conformations generated is done solely on the basis of energy, for internal (core) residues, since good van der Waal's interactions are considered to be equal to a good packing of the sidechains. The situation becomes more complicated when trying to predict the conformation of surface residues. The lowest van der Waal's interaction is obtained by a combination of sidechain conformations which minimize the overlap of atoms, this means that the lowest energy is obtained with extended conformations of sidechains, without considering good packing of sidechains.

[0087] Using the fact that hydrophobic, bulky residues will be shielded by the hydrophilic sidechains, and will be buried in the surface, it is possible to generate a simple function which will evaluate these macroscopic observations. These functions can either be implemented in the objective evaluation function of the Monte Carlo simulation, or as is

done here, added as a post processing step. Including an accessibility/hydrophobicity term in the evaluation function would slow down the calculation considerably, hence the term has been added as a post processing function. The function used is a sum of the product of relative exposed surface area multiplied by the residual hydrophobicities. The hydrophobicities used are taken from Cornette et al. (Cornette et al., 1987).

$$f_{conformation} = \sum_{i=1}^{n} -A_{irel} \cdot H_{irel}$$

n is the number of sidechains reconstructed. The surface area is calculated using the tesselated icosahedron approach (Chau and Dean, 1987), which is not very precise (0.1 percent), but is able to evaluate a large number of conformations. The function is evaluated for the final 2,000 conformations and the lowest value conformation selected as the best.

[0088] Using this simple approach it is possible to integrate over a large phase space with many degrees of freedom, and get a complete sampling of the space.

Predicted Structures of an Anti-hapten, Anti-peptide and Two Anti-protein Antibodies

20 [0089] In the following section the predicted structures of four different antibody F_v regions are presented and analyzed. The antibodies are:

- Gloop-2 (Darsley and Rees, 1985), an anti-lysozyme antibody whose Fab structure was determined by Jeffrey et al., (Jeffrey et al., 1991) and which was used as a learning exercise during the development of CAMAL.
- D1.3 (Amit et al., 1986), an anti-lysozyme antibody whose uncomplexed F_v coordinates were supplied by R. Poljak
 et al. after the model coordinates had been deposited.
- 36-71 (Rose et al., 1990), an anti-phenylarsonate antibody whose Fab structure was carried out by D. R. Rose, et al., and whose coordinates were obtained after the model coordinates had been deposited.
- 3D6 (Grunow et al., 1988), an anti-protein (GP41 of HIV) antibody whose Fab structure was carried out by D. Carter et al. (Carter, 1991) and whose coordinates were obtained after the model coordinates had been deposited. For this antibody, the model was generated using the canonical loop method of Chothia & Lesk (Chothia et al., 1989; Chothia et al., 1986) for CDRs L1, L2, H1 and H2, while L3 and H3, which cannot be modelled using canonical structures, were constructed using CAMAL.

[0090] All four models were subjected to both restrained and unrestrained energy minimization using the DISCOVER (TM Biosym Technology) potential with 300 cycles of steepest descents, followed by conjugate gradient minimization until convergence to within 0.042J (0.01 Kcal) occurred.

[0091] The resolution and R-factors of the x-ray structures are given in Table 3 together with the parent frameworks selected in building the models. The structures and models were compared by global fits of the loops. The β -barrel strands 1 to 6, as described above, were least squares fitted and the RMS deviation was then calculated over the loops. The backbone (N,C α ,C) RMS values for fitting model and crystal structure frameworks were between 0.4 and 0.9x10⁻¹⁰m (0.4 and 0.9 Å), illustrating the conservation of the core β -barrel. Using all eight strands RMS deviations between 0.6 and 1.2x10⁻¹⁰m (0.6 and 1.2 Å) were observed.

[0092] Global fits (Table 4) give a more realistic measure of the accuracy of the model than a local least-squares fit over the loops since they account for the overall positioning of the loops in the context of the F_v structure. Local fits, which give lower RMS deviations, are also shown in Table 4. Differences between local and global RMS deviations arise from differences in V_H/V_L domain packing and differences in loop 'take off' angles and positions.

[0093] Table 5 shows the canonical loops selected from modelling 3D6. Backbone structures of the modelled CDRs, superimposed on the x-ray structures after global fitting are shown in Figure 8. General features and points of interest for each of the six CDRs are discussed below.

5 Analysis of the CDR Regions

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[0094] During the comparison of CDR conformations in the V-region models and the x-ray Fab structures it was observed that at certain positions in a CDR, the peptide backbone may adopt either of two conformations by undergoing

a "peptide flip" (1,4 shift). This phenomenon is also seen in type 2 β -turns (Paul et al., 1990). Dynamics simulations of β -turns show that the transformation energy between $\phi 1 = -00$, $\psi 1 = -30$, $\phi 2 = -90$, $\psi 2 = 0$ and $\phi 1 = -00$, $\psi 1 = 120$, $\phi 2 = 90$, $\psi 2 = 0$ has a maximum value of 5 kcal (Paul et al., 1990). This is low enough to allow selection of either conformation. The peptide flip is observed within several canonical classes (as described by Chothia et al. (Chothia et al., 1989)) and the hydrogen bonding pattern used to determine the conformation of a canonical class does not disallow the peptide flip. Any modelling procedure should therefore take these, or any other multiple conformations, into consideration where the transformation energies are sufficiently low to permit population of the different conformational forms. Table 6 shows an example of the "peptide-flip" phenomenon from the crystallographic database of antibody structures. It should be noted that a single crystal structure will not show multiple conformations since the crystallization will 'freeze out' one of the conformations. During the modelling procedure the two populations of conformers are easily extracted from a set of ab initio generated loops, by using a torsional clustering algorithm.

CDR-L1

[0095] In Gloop-2 and D1.3, all five low energy conformations were very similar with RMS deviations differing by less than 0.25x10⁻¹⁰m (0.25 Å) (backbone) and 0.35x10⁻¹⁰m (0.35 Å) (all atoms). The FILTER algorithm was unable to distinguish between the conformations and the lowest energy structure was selected.

[0096] Although CDR-L1 of 3D6 was originally built using the canonical loop from HyHEL-10, the midsection was rebuilt by conformational search, for the following reason. HyHEL-10 and REI CDR-L1 loops are placed in the same canonical ensemble (Chothia et al., 1989) although they contain a 1-4 shift (peptide flip) relative to one another between the fifth and eighth residues of the loop (residues 28-31) (see Table 6).

[0097] 36-71 shows the same 1-4 shift between the model and crystal structure CDRs. Both crystal structure and model were compared with other loops of the same canonical class as defined by Chothia et al. (Chothia et al., 1989). It was found that the hydrogen bonding pattern which determines the conformation was conserved.

CDR-L2

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[0098] CDR-L2 of D1.3 has two adjacent threonines (49, 50) which in the x-ray structure are packed against the tyrosine at the fourth position of CDR-H3, thus minimizing the exposed hydrophobic sidechains. In the unminimized model the threonine sidechains are exposed to the solvent, but after energy minimization, this packing is observed.

CDR-L3

[0099] In Gloop-2, D1.3 and 36-71 the proline at the seventh position in the loop is correctly predicted in the *cis* conformation. It has previously been suggested that the conformation of CDR-L3 is dictated by the presence of a proline in position 8 or 9 (Chothia et al., 1989) within the loop. 3D6 does not have a proline in either position. Only 7 out of 290 CDR-L3 sequences (Kabat et al., 1987) lack a proline at both positions and in all of the published x-ray structures this proline is present. This is an example of a situation where either a new canonical class may need to be defined or where the canonical rule breaks down altogether, and an alternative method must be employed.

[0100] The 3D6 L3 loop is 7 residues in length and was built using database loops alone where conformational space is saturated by means of fragments selected from the crystallographic database (Global RMS $2.01 \times 10^{-10} \text{m}$ (2.01 Å), N,C α ,C), and by using CAMAL (Construction: Q[Q(YNS)Y]S, Global RMS: $1.97 \times 10^{-10} \text{m}$ 1.97 Å, N,C α ,C). The similarity of the structures generated by the two procedures illustrates the utility of the database search and suggests that, for shorter loops it is capable of saturating the available conformational space.

CDR-H1

[0101] Using the Kabat and Wu definition of CDR-H1 places this loop as an extension of the β-sheet. The extended nature of this stretch of peptide limits its conformational flexibility and CDR-H1 is generally modelled accurately (Martin et al., 1989; Chothia et al., 1989).

[0102] In Gloop-2 and D1.3, the Phe or Tyr sidechain at the second position in the loop is poorly placed and packs against Leu at the penultimate position in HFR1 (see Table 2). 36-71 has a well-placed Asn at this position, rather than the more common bulky hydrophobic sidechain.

55 CDR-H2

[0103] CDR-H2 of 36-71 is similar in sequence to F19.9 (Strong et al., 1991), (36-71: YNNPGNGYIA (SEQ ID NO: 492); F19.9: YINPGKGYLS (SEQ ID NO:493)). While the structurally determining residues specified by Chothia and

Lesk (Chothia et al., 1989) are conserved, the backbone conformations are different: F19.9 has a bulge at the -PGN-Gly, compared with 36-71, giving the loop a 'kink' in the middle. The model of 36-71 shows a 1-4 shift, though the sidechains are still well placed.

[0104] In Gloop-2, the all atom RMS deviation is poor $(3x10^{-10}\text{m})$ (3.00 Å) (Jeffrey et al., 1991) when compared with the P2₁ crystal structure, owing to rotations of the Phe at position 3 in the loop and Tyr at position 10 by approximately 120° about the χ_2 torsion angle. Gloop-2 has been solved in two different crystal forms, P2₁ and P1 (Jeffrey et al., 1991; Jeffrey, 1989). When compared with the P1 structure, the sidechains are placed almost perfectly and the all atom RMS (global fit) drops to 2.23x10⁻¹⁰m (2.23 Å).

[0105] This concerted sidechain motion between crystal forms illustrates the effects of crystallization conditions on surface sidechain placement. Even though surface sidechains may show low temperature factors indicating low mobility in the crystal, their mobility in solution may be high. In the Gloop-2 P1 structure, the mean sidechain temperature factor for the F_v domain is 13.46 (σ = 8.20) while the sidechains of these two residues of H2 show mean temperature factors of 5.56 (σ = 0.68) for the Phe at position 3 and 7.10 (σ = 1.73) for the Tyr at position 10.

CDR-H3

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[0106] CDR-H3 is the most variable of the six CDR's with all lengths up to 21 residues being represented in Kabat et al., (Kabat et al., 1987). This extreme variability results from V-D-J splicing (Schilling et al., 1980) and has always been a problem when attempting to model antibodies. Such loops may be divided into short (up to 7 residues), medium (up to 14 residues) and long (15 or more residues). Using the CAMAL procedure, short and medium CDR-H3's can be modelled as accurately as other CDR's of similar lengths. Although long CDR-H3's are more difficult and cannot, at present, be built to the same accuracy, the chain trace is still correct.

[0107] It is unlikely that the longer loops consist of 'pure' loops (i.e., all random coil or turn). In crystal structures of antibodies with medium to long CDR-H3 loops (McPC603 (Rudikoff et al., 1981): 11 amino acids (aa); KOL (Marquart et al., 1980): 17 aa; F19.9 (Lascombe et al., 1989): 15 aa) the loops consist of a disordered β-sheet extension from the β-barrel core and a 5-8 residue random coil/turn connecting these two strands.

[0108] To determine the nature of medium to long loops (>8 residues) which satisfy the CDR-H3 constraints, a complete search of the Protein Databank for loops of length 8-20 residues, was performed using the inter-Cα distance constraints determined from known antibody crystal structures for CDR-H3. The resulting loops were then analyzed using the DSSP (Kabsch and Sander, 1983) program, which is able to assign secondary structure to polypeptide structures. The amount of secondary structure for each length of loop was calculated, and it was observed that for loops longer than 12 residues the amount of secondary structure within each of the classes described in DSSP was constant. The number of loops selected is also constant (approximately 150 loops) for loops longer than 12 residues. A closer inspection of each of the length ensembles shows indeed that the loops are the same between the groups.

[0109] This analysis shows that, like the long CDR-H3 crystal structures, the selected fragments consist of β -strands connected by 5-8 residue loops. For loops above 12-13 residues in length, the same loops are selected, but with extensions to the β -strands. This is called the "sliding-ladder" effect. In addition, the maximum size of a random coil or turn fragment in any of the structures contained in the Protein Databank tends not to exceed 8 residues, as determined by DSSP. This implies that the conformational space of longer loops is not saturated by the database and, although it is unlikely that long loops in antibodies will differ significantly from long loops in other structures, confidence in the prediction must be correspondingly reduced.

[0110] By how much is the usefulness of the CAMAL algorithm reduced by this observation?

[0111] The frequency of occurrence of different CDR-H3 lengths in antibody sequences described by Kabat et al. (Kabat et al., 1987) was analyzed. Figure 10 shows that more than 85% of H3 loops have lengths between 4 and 14 residues which can be modelled accurately by the CAMAL algorithm.

[0112] CDR-H3 of D1.3 is of average length (8 residues), though no loops of this length are seen in the available antibody structures. The crystal structure coordinate set showed an RMS of 1.9x10⁻¹⁰m (1.9 Å) compared with the model.

[0113] The 36-71 loop is 12 residues long. The conformation is correctly predicted as a short loop connecting an extension of the β -sheet.

[0114] The 3D6 H3 loop is 17 residues long. While KOL (Marquart et al., 1980) has the same length it has only one residue in common with 3D6 and only one conservative mutation. There is thus no reason to believe that the conformations would be similar. The final predicted conformation of 3D6 is an extended β-sheet, as in the crystal structure. The difference between the predicted and the crystal structure of 3D6-H3 is due to a twist of 5-7° in the extended β-sheet loop (see Figures 9A-9D). Such a twist has also been observed for complexed and uncomplexed antibodies by Wilson et al. (Wilson and others). This suggests that long CDR-H3 loops may be flexible and actively involved in antigen binding.

The Complete Variable Region

[0115] Prediction of the strand positions and V_L - V_H orientation in the framework β-barrel was exact for all of the four antibodies. The backbone (N,Cα,C) RMS deviations from the crystal structures were between 0.56 and 0.86x10⁻¹⁰m (0.56 and 0.86 Å), despite the fact that, in all cases the V_L and V_H regions of a particular model were derived from different antibody structures. This suggests that this method will do well in procedures such as humanization (German et al., 1991), where correct framework positioning is important. The backbones of all six CDRs in all four antibodies are essentially correctly predicted, as shown in Figure 8. There are two important points to make about these predictions. First, the position of each CDR on its framework barrel is correct. Thus, CDR-framework interactions can be confidently monitored. The only deviation from the x-ray structure is CDR-H3 of antibody 3D6 which has been previously discussed. Second, the all atom RMS deviation between models and x-ray structures is dominated by sidechain positions. In most instances this deviation is due to a small number of incorrectly positioned, exposed sidechains (for example, in D1.3 the only sidechains which are incorrectly predicted are Tyr 9 of L1, Trp 4 of L3, Tyr 2 of H1 and Tyr 4 of H3). Since each CDR is constructed in the absence of other CDRs, the force field may choose a rotamer which is 120° away from that found in the crystal structure. This effect has also been observed by Lee et al. (Lee and Levitt, 1991).

Conclusion

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- [0116] For antibodies having CDR H3 regions of 14 residues or less the complete variable domain can be modelled to an accuracy approaching that of medium resolution x-ray structures. For antibodies with longer H3 loops the CAMAL algorithm is likely to need an additional procedure in which molecular dynamics simulations are also incorporated.

 [0117] The canonical approach of Chothia et al. appears to work well (at least in modelling backbones) where it may be applied and may be used successfully in combination with the CAMAL procedure.
- [0118] One important observation that has emerged from these studies is that a given loop can exist in several conformations. In particular, this seems likely for CDR-L1 and, to a lesser extent, CDR-L3 and longer CDR-H3's. A simple combinatorial calculation shows that, if each of these three loops can exist in three separate conformations, a given combining site can have 3³ = 27 different topographies. Clearly, this would explain the origins of cross reactivity and would allow for induced fit of antigens.

Anihody SEQ 11 DIQMTQSPSUSASUGENVSITCRASQUIHH 12 DIQMTQSPSUSASUGENVSITCRASQUIHH 13 DIQMTQSPSUSASUGENVSITCRASQUIHH 14 DIQMTQSPSUSASUGENVSITCRASQUIHH 15 DIQMTQSPSUSASUGENVSITCRASQUIHH 16 DIQMTQSPSUSASUGENVSITCRASQUIHH 16 DIQMTQSPSUSASUGENVSITCRASQUIHH 17 DIQMTQSPSUSASUGENVSITCRASQUIHH 18 DIQMTQSPSUSASUGENVSITCRASQUIHH 19 DIQMTQSPSUSASUGENVSITCRASQUIHH 10 DIQMTQSPSUSASUGENVSITCRASQUIHH 11 DIQMTQSPSUSASUGENVSITCRASQUIHH 12 DIQMTQSPSUSASUGENVSITCRASQUIHH 13 DIQMTQSPSUSASUGENVSITCRASQUIHH 14 DIQMTQSPSUSASUGENVSITANGUIHH 15 DIQMTQSPSUSASUGENVSITANGUIHH 16 DIQMTQSPSUSASUGENVSITANGUIHH 16 DIQMTQSPSUSASUGENVSITANGUIHH 17 DIQMTQSPSUSASUGENVSITANGUIHH 18 DIQMTQSPSUSASUGENVSITANGUIHH 18 DIQMTQSPSUSASUGENVSITANGUIHH 18 DIQMTQSPSUSASUGENVSITANGUIHH 19 DIQMTQSPSUSASUGENVSITANGUIHH 10 DIQMTQSPSUSASUGENVSITANGUIHH 10 DIQMTQSPSUSASUGENVSITANGUIHH 11 DIQMTQSPSUSASUGENVSITANGUIHH 12 DIQMTQSPSUSASUGENVSITANGUIHH 13 DIQMTQSPSUSASUGENVSITANGUIHH 14 DIQMTQSPSUSASUGENVSITANGUIHH 15 DIQMTQSPSUSASUGENVSITANGUIHH 16 DIQMTQSPSUSASUGENVSITANGUIHH 16 DIQMTQSPSUSASUGENVSITANGUIHH 16 DIQMTQSPSUSASUGENVSITANGUIHH 17 DIQMTQSPSUSASUGENVSITANGUIHH 18 DIQMTQSPSUSASUGENVSITANGUIHH 18 DIQMTQSPSUSASUGENVSITANGUIHH 19 DIQMTQSPSUSASUGENVSITANGUIHH 10 DIQMTQSPSUSASUGENVSITA	indicates strands is one of the	Table 2:		3671	gloop-3	3D4	3071	gloop-2	Autibody	300	3671	619	gioop-2	į	JD4	3671	gloop-7		Antibody
Tegions; + for \$\beta\$-es + \cdot \	β-strain (Η or heav)	Alignn	5	=	u -	5	<u>-</u> "	-	SEQ Pas	13	=	<u>.</u>	-	;		= `	, ~		SEQ Pas
+3334	nd regions used in the fitting for modelling frameworks. Nomenclature for β -barrel Γ L - Chain) - FR(Framework region)-(Strand number), thus for example strand y chain becomes HFR1.	nent of antibody sequences used in the modelling. '*' indicates CDR, regions; '+'	CHARACTER ROMARNS OF FORMAS FRANCIS OF FOR FORMAS FRANCIS OF FOR FOR FOR FOR FOR FOR FOR FOR FOR	-TYZEXPXQXTTLTVDXSSXTAYMQLRSTLSBDSAVYPCARSBYYQQSYXTDYX	TOYNSALKSACS-SKONKSOVFLKMNSCHTDDTARYYCARBRDYRC	VQLVESGGGLVQPGRSLRLSCAASGPTPNDYAMH WVRQAPQRGLEWVSG1SWDSS.	VOLCOSOVELVAAOSSYKMSCKASOVITIUNGIN. WYKORPOOGLEWIGYNNYGNO.	. SKOJE I BOLMBIO O O LILO LILO LILO LILO SKAJE SKAJE LILO SCOLO SKOJE LILO SCOLO SKOJE SKAJE LILO SCOLO SKOJE SKAJE SKOJE SKO		SOVES RESOSOR CETCHES SUPPORATE COOPENS WEEDFORK OF KE	SOVPSRPSOSOSOTOVSCTISNLEQEDIATYPCQQONALPRTPGQGTKL81KR	DOVPSHESOSOTOYSLKINGLQPEDPOSYYCQHEWSTPATFOGOTKLEIKA	SQVPXRPSQRRSQSDVSCTI-S&CRBBDTADTYCTCVC4 YPCHPQAQTXCTTCXP			- CATO TANGETON CONTRACT TO SECURITION OF THE PROPERTY OF THE	TOWTOSPSSES ASCORNISCITORA SOCISCITO YESWLOOKPOOTIKRE IYAAST	**************************************	

Table 3:

	to build the models.	Resolution data for D1.3 h	ias not yet been publish	ea.
-			Framew	ork Model
Antibody	Resolution	R-factor	Light	Heavy
Gloop-2	2.80	21.2	REI	HyHEL-5
D1.3	-	· -	REI	NEW
36-71	1.90	20.9	Gloop2	NEW
3D6	2.70	17.7	REI ,	KOL

					KM3 IOCAL	0041 (A)			The state of the s	•	
Antibody	CDR	eequence	ON GI Das	Co	N,Ca,C	VII CO	All MC	Ca	N,Co,C	-	AU MC
Glass.2	=	BASIOFEISIGIVES		0.73	0.71	3.08	-	:	0.97	2.00	2.13
20.5		MACIONIMINALA		2.2		4.34	3.54	2.73	3.8	1.85	4.83
36-71		BAGODENE STA	496	3.71	2.63		4.60	18.6	8.81	8.10	8.07
306		RASIQ(SIO)NINLH	497	0.81	0.84	2.40	1.63	20.0	0.78	2.00	=
	,				•		3				
Croop-3	L)	AASTLDS		0.20	0.40	0.00	1.00				
. DI.3	•	YIT(TTL)AID	100	0.47	0.73	1.00	1.40	0.50	1.03	2.01	1.71
36-71		PIT(SRS)QIS	500	0.44	0.0	2.34	3.28	0.78	0.73	2.43	3.40
3D6		KASSLEŚ	108	0.41	0.42	1.37	1.20	0.83	0.00	1.78	1.00
						•	;	:		•	5
		041 (80) 0 ·			200		3	74	1.70		3.30
30-71		COLONALIBIAT	504	1.00	1.00	2.26	2.10		1.36	2.17	2.20
3D6		OIQ(YNS)YIS	508	1.46	1.00	D.04	3.90	2.31	1.97	2	3.88
2		TEONT			3	3		1.03	-	20	2.00
Dis		G(YGY)	807	0	0.83	2.38	2.00	9. 8	0.00	5.24	2.01
36-71		SCHOLINE	500	9	0.8	2.22	:::	1.00	0.07	2.01	2.23
3D6		DYAMH	809	0.07	0.77	1.63	1.11	0.01	0.72	1.69	1.20
Ginen.	3	EUF/PON)SIXTY	910	0.63	•	-	1.70	1.20	0.0	2.28	9.10
D1.3		MIWGDONTD	511	0.42	0.13	1.55	1.60	0.87	0.88	1.00	
36-71		YNNIP(GNG)YJIA	613	0.04	0.78	2.01	3.30	1.47	1.41	1.70	1.00
306		ISWDSSSIG	513	0.48	0.82	2.88	2.00	0.08	0.00	2.68	2.10
Glosp-2	£	R(EIR)Y	9 .	0.00		9.0	2	0.87	1.07	9.0	
01.3		ERIDIYRLIDIY	318	0.50	0,83	-	1.20	1.28	0.01		1.38
36-71		SEYY[O(OSY)K]PDY	. 916	1.98	1.78	4.40	4.00	2.00	2.88	•	0.00
306		GROYYID(SQQ)YFITVAPDI	317	9.66	3.13	5.83	1.01	4.80	3.98	9.30	8.20

calculating the RMS over the loops. The total RMS of the frameworks (N,Ca,C) is 0.81, 0.60, calculated by least-squares fitting the conserved core of the two structures upon each other and difference between model and crystal structure loop coordinates. The RMS values are a global fit 0.86 and 0.56 respectivly =construction area, ()= Chain closure, all sidechains are constructed. RMS(Root Mean Square) Table 4: Sequence and conformational search construction scheme for each of the 24 CDRs,

Loop	Canonical	Sequence	SEQ ID NO
Li	HyHEL-10	RASQSISRWLA	518
	(3D6)	RASQSIGNNLH	497
L2	REI	EASNDLA	519
•	(3D6)	KASSLES	501
H1	McPC603	DFYME	520
	(3D6)	DYAME	509
H2	KOL	I I WD DG S DQ""	521
	(3D6)	ISWDSSSIG	513

Table 5: Canonical loops selected for the model of 3D6(taken from Chothia et al (1989)).

Table 6:

				la la	ible 6:			
20	Backbone ¢	, ,			•	d REI classified ptide flip are ind		nonical group
	Residue	Number	24	25	26	27	28*	29*
25	REI	Sequence φ/ψ	Q -/138	A-103/157	S -96/7	Q -158/142	S -40/108	I 112/9
	HyHEL-10	Sequence φ/ψ	R -/108	A -85/135	S -88/64	Q 172/160	S -64/-38	I 9/63
	Residue	Number	30*	31*	32	33	32	
30	REI	Sequence φ/ψ	1 79/-77	K -146/21	Y -104/89	L -143/133	N -144/-	SEQ ID NO: 522
	HyHEL-10	Sequence φ/ψ	G -63/107	N 85/-15	N -105/12	L -129/118	H -126/-	SEQ ID NO: 518

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	Asp II	e Gl	n Me	t Th	r G1: 5	n Se	r Pro	Se:		r Le 10	u Se	er Al	.a Se	er Le	eu Gl 15	Y
5	Glu	ı Arg	Val	Ser 20	Leu	Thr	Cys	Arg	Ala 25		Gln	Glu	Ile		Gly 30	Tyr
10	Lev	Ser	Trp 35	Leu	Gln	Gln	Lys	Pro 40		Gly	Thr	Ile	_	Arg 5	Leu	Ile
15 .	Tyr	Ala 50		Ser	Thr	Leu	Asp 55		Gly	Val	Pro	Lys 6	_	Phe	Ser	Gly
	Arg 65	Arg	Ser	Gly	Ser	Asp 70	Tyr	Ser	Leu	Thr	Ile 75	Ser	Ser	Leu	Glu	Ser 80
20 .	Glu	Asp	Phe	Ala	Asp 85	Tyr	Tyr	Cys	Leu	Gln 90		Leu	Ser	Tyr		Leu 5
25	Thr	Phe	Gly	Ala 100	Gly	Thr	Lys	Leu	Glu 105		. Lys	Arç	, Ala	a		
	(2) INFO	DRMAT	ION FO	OR SE	O ID N	O:2							•			
30	(i) S	EQUE	NCE C	HARA	CTERI	STICS	: -									
		(A) LEI (B) TY (C) TO	PE: am	nino ac	id	cids										

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

	Asp 1	Ile	Gln	Met	Thr 5	Gln	Ser	Pro	Ala	Ser 1		Ser	Ala	Ser	Val	Gly L5
5 ′	Glu	Thr	Val	Thr 20	Ile	Thr	Cys	Arg	Ala 29		Gly	Asn	Ile		Asn 0	Tyr
10	Leu	Ala_	Trp 35	Tyr	Gln	Gln	Lys	Gln 40		Lys	Ser	Pro		Leu 5	Leu	Val
15	Tyr	Tyr 50	Thr	Thr	Thr	Leu	Ala 55		Gly	Val	Pro	Ser 6		Phe	Ser	Gly
	Ser 65	Gly	Ser	Gly	Thr	Gln 70	Tyr	Ser	Leu	Lys	Ile 75	Asn	Ser	Leu	Gln	Pro 80
20	Glu	Asp	Phe	Gly	Ser 85	Tyr	Tyr	Cys	Gln	His • 9		Trp	Ser	Thr	Pro 9	Arg 5

Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys Arg Arg 100 105

(3) INFORMATION FOR SEQ ID NO:3

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 107 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

	Asp 1	Ile	Val	Leu	Thr 5	Gln	Ser	Pro	Ala	Ile 1		Ser	Ala	Ser		Gly .5
	Glu	Lys	Val	Thr 20	Met	Thr	Cys	Ser	Ala 25		Ser	Ser	Val		Tyr 0	Met
10	Tyr	Trp	Tyr 35	Gln	Gln	Lys	Ser	Gly 40		Ser	Pro	Lys		Trp 5	Ile	Tyr
15	Asp	Thr 50	Ser	Lys	Leu	Ala	Ser 55		Val	Pro	Val		Phe 0	Ser	Gly	Ser
	Gly 65	Ser	Gly	Thr	Ser	Tyr 70	Ser	Leu	Thr	Ile	Ser 75	Ser	Met	Glu	Thr	Glu 80
20	Asp	Ala	Ala	Glu	Tyr 85	Tyr	Cys	Gln	Gln	Trp		Arg	Asn	Pro	Thr	Phe 5
25	Gly	Gly	Gly	Thr 100	Lys	Leu	Glu	l Ile	Lys 105		y Ala	a				
	(4) INF	ORMAT	TION F	OR SE	EQ ID I	NO:4					:					
30	(i) ⁵	(B) T	ENCE (ENGTH YPE: a: OPOLO	l: 109 a mino a	amino cid		S: .				;					
35	(ii)	MOLE	CULE	TYPE:	peptid	le										, '
	(xi)	SEQU	IENCE	DESC	RIPTI	ON: SI	EQ ID	NO:4:								
40	Asp 1	Ile	Val	Leu	Thr 5		Ser	Pro	Ala	Thr 1	Leu 0	Ser	Val	Thr	Pro 1	Gly 5
45													•			

_	Asn	ser	Val	Ser 20		Ser	Cys	Arg	Ala 2		Gln	Ser	Ile		Asn 80	Asn
5	Leu	His	Trp 35	Tyr	Gln	Gln	Lys	Ser 40		Glu	Ser	Pro	_	Leu 5	Leu	Ile
10	Lys	Tyr 50	Ala	Ser	Gln	Ser	Ile 55		Gly	Ile	Pro	_	Arg O	Phe	Ser	Gly
15	Ser 65	Gly	Ser	Gly	Thr	Asp 70	Phe	Thr	Leu	Ser	Ile 75	Asn	Ser	Val	Glu	Thr 80
	Glu	Asp	Phe	Gly	Met 85	Tyr	Phe	Cys	Gln	Gln 9		Asn	Ser	Trp	Pro 9	Tyr 5
20	Thr	Phe	Gly	Gly 100	Gly	Thr	Lys	Leu	Glu 105		Lys	Arq	, Ala	a		
	(5) INF	ORMA	TION I	FOR S	EQ ID	NO:5										
25	(i) :	SEQUE	ENCE	CHAR	ACTE	RISTIC	cs:									
		(B) T	ENGTI YPE: a OPOL	mino a		acids										-
30	(ii)	MOLE	CULE	TYPE	: peptic	de										
	(xi)	SEQL	JENCE	DESC	CRĮPT	ION: S	EQ ID	NO:5	:					•		
35	Glu 1	Ile	Val	Leu	Thr 5		Ser	Pro	Ala	Ile 1	_	Ala	Ala	Ser	Leu 1	Gly .5
40	Gln	Lys	Val	Thr 20	Ile	Thr	Cys	Ser	Ala 25		Ser	Ser	Val		Ser 0	Leu
45	His	Trp	Tyr 35	Gln	Gln	Lys	Ser	Gly 40		Ser	Pro	Lys		Trp 5	Ile	Tyr
	Glu	Ile 50	Ser	Lys	Leu	Ala	Ser 55		Val	Pro	Ala		Phe 0	Ser	Gly	Ser
50	Gly 65	Ser	Gly	Thr	Ser	Tyr 70	Ser	Leu	Thr	Ile	Asn 75	Thr	Met	Glu	Ala	Glu 80
	Asp	Ala	Ala	Ile	Tyr 85	Tyr	Cys	Gln	Gln	Trp 90		Tyr	Pro	Leu	Ile 9	Thr 5
55																

Phe	Gly	Ala	Gly	Thr	Lys	Leu	Glu	Leu	Lys	Arg	Ala
			100					105			

5	(6) INFORM	MATION F	OR SEC	ON DI C	:6			,						
	(i) SEC	UENCE (CHARAC	CTERIS	TICS:									
10	(B)	LENGTH TYPE: ar	mino aci	id	ds									
	(ii) MO	LECULE	TYPE: p	eptide										
15	(xi) SE	QUENCE	DESCR	RIPTION	: SEQ ID	NO:6:								
20	Glu Se	er Val	Leu	Thr G	ln Pr	o Pro	Ser	Ala 10		Gly	Thr	Pro	_	Gln 15
25	Arg Va	al Thr	Ile 20	Ser C	ys Th	r Gly	Thr 2		Ser	Asn	Ile	_	Ser 0	Ile
,	Thr Va	al Asn 35	-	Tyr G	iln Gl	n Leu 4		Gly	Met	Ala		Lys 5	Leu	Leu
30	_	r Arg	Asp	Ala M		g Pro 55	Ser	Gly	Val		Thr O	Arg	Phe	Ser
35	Gly Se	er Lys	Ser	Gly I	hr Se 70	r Ala	Ser	Leu	Ala 75	Ile	Ser	Gly	Leu	Glu 80
	Ala G	lu Asp	Glu	Ser A	sp Ty	r Tyr	Cys	Ala 90		Trp	Asn	Ser		Asp 5
40	Asn Se	er Tyr	Val 100	Phe G	ly Th	r Gly	Thr 10		Val.	Thr	Val	. Leu 11		Gln
45	(7) INFORI	MATION F	OR SE	Q ID NO	:7									
	(i) SEC	QUENCE (CHARAG	CTERIS	TICS:									

- (A) LENGTH: 115 amino acids

- (B) TYPE: amino acid (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

	Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ala Gly 1 5 10 15
5	
10	Glu Arg Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Se 20 25 30
	Gly Asn Gln Lys Asn Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gl 35 40 45
15 `	Pro Pro Lys Leu Leu Ile Tyr Gly Ala Ser Thr Arg Glu Ser Gly Va: 50 55 60
20	Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr 65 70 75 80
	Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asr 85 90 95
25	Asp His Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile 100 105 110
30	Lys Arg Ala 115
	(8) INFORMATION FOR SEQ ID NO:8
. 35	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 103 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:
45	

	Ser 1	Val	Leu	Thr	Gln 5	Pro	Pro	Ser	Val		Gly 0	Ala	Pro	Gly		Arg L5
5	Val	Thr	lle	Ser 20	Cys	Thr	Gly	Ser	Ser 2		Asn	Ile	Gly		Gly 80	Asn
10	His	Val	Lys 35	Trp	Tyr	Gln	Gln	Leu 40		Gly	Thr	Ala	Pro	Lys 15	Leu	Leu
15	İle	Phe 50	His	Asn	Asn	Ala	Arg 55		Ser	Val	Ser		Ser 0	Gly	Ser	Ser
,	Ala 65	Thr	Leu	Ala	Ile	Thr 70	Gly	Leu	Gln	Ala	Glu 75	Asp	Glu	Ala	Asp	Tyr 80
20																
25	Ty	r Cys	s Gln	Ser	Tyr 85		Arg	Ser	Leu	Arg 90	Val	Phe (Gly (Gly o	95	
	Ly	s Lev	ı Thr	Val 100		Àrg	Gln									
30	(9) IN	FÖRMA	ATION I	FOR S	EQ ID	NO:9										
	(i)	SEQU	ENCE	CHAR	ACTE	RISTIC	S:									,
35		(B) T	ENGTI YPE: a OPOL	mino a	acid	acids										
-	(ii) MOLE	CULE	TYPE	: peptio	de										
40	(x	i) SEQI	UENCE	DES	CRIPT	ION: S	EQ ID	NO:9:		٠.						

	Asp 1	Val	Val	Met	Thr 5	Gln	Thr	Pro	Leu	Ser 1		Pro	Val	Ser	Leu 1	Gly. LS
	Asp	Gln	Ala	Ser 20	Ile	Ser	Cys	Arg	Ser 25	_	Gln	Ser	Leu		His O	Ser
10	Gln	Gly	Asn 35	Thr	Tyr	Leu	Arg	Trp		Leu	Gln	Lys		Gly 5	Gln	Ser
	Pro	Lys 50	Val	Leu	Ile	Tyr	Lys 55		Ser	Asn	Arg		Ser O	Gly	Val	Pro
15	Asn 65	Arg	Phe	Ser	Gly	Ser 70	Gly	Ser	Gly	Thr	Asp 75	Phe	Thr	Leu	Lys	Ile 80
20	Ser	Arg	Val	Glu	Ala 85	Glu	Asp	Leu	Gly	Val	Tyr)	Phe	Cys	Ser	Gln 9	Ser 5
	Thr	His	Val	Pro 100	Trp	Thr	Phe	Gly	Gly 105		Thr	Lys	Leu	Glu 11	Ile O	Lys
25	Arg	: Ala														
					•											
	(10) INI		ATION	FOR	SEQ II	D NO:	 10									
30	(10) INI (i) \$										- 1					
		FORM. SEQUI (A) LI (B) T	ENCE	CHAR H: 109 nmino a	ACTE amino	RISTI	CS:									
	(i) \$	FORM. SEQUI (A) LI (B) T	ENCE ENGTI YPE: a OPOL	CHAR H: 109 amino a OGY: I	ACTE amino acid inear	RISTIO	CS:				*					
	(i) \$ (ii)	FORM SEQUI (A) LI (B) T (C) T	ENCE ENGTH YPE: a OPOL	CHAR H: 109 Imino (OGY: I TYPE	ACTE amino acid inear : pepti	RISTIO acids	CS:) NO:1	0:		· ·				, a	

	Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly 1 5 10 15	
5	Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30	
	Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Val 35 40 45	
15	Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60	
	Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu His 65 70 75 80	
20	Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Ser Thr Thr Pro Arg 85 90 95	
25	Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Arg 100 105	
	(11) INFORMATION FOR SEQ ID NO:11	
30	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 109 amino acids	
	(B) TYPE: amino acid (C) TOPOLOGY: linear	
35	(ii) MOLECULE TYPE: peptide	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:	
40	Asp Ile Gln Met Thr Gln Ile Pro Ser Ser Leu Ser Ala Ser Leu Gly 1 5 10 15	
45	Asp Arg Val Ser Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Phe 20 25 30	
	Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Ile Lys Leu Leu Ile 35 40 45	
50	Tyr Phe Thr Ser Arg Ser Gln Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60	

	Ser 65	_	Ser	Gly	Thr	Asp 70	Tyr	Ser	Leu	Thr	11e 75	Ser	Asn	Leu	Glu	Gln 80
5	Glu	Asp	Ile	Ala	Thr 85	Tyr	Phe	Cys	Gln	Gln 90		Asn	Ala	Leu	Pro 9	Arg 5
10	Thr	Phe	Gly	Gly 100	Gly	Thr	Lys	Leu	Glu 105		Lys	Arg	, Ala	1		
	(12) INF	ORMA	TION F	OR SE	Q ID I	NO:12			•							
15	· (i) S	EQUE					:									
		(B) TY	NGTH: PE: am POLO	ino aci	id	cids										
20	(ii) I	MOLEC	ULE T	YPE: p	eptide				·							
	(xi)	SEQU	ENCE [ÉSCF	RIPTIO	N: SEC	Q ID N	O:12:								
25	Asp	lle	Gln	Met	Thr	Gln ;	Ser	Pro	Sei		Leu 10	ı Se	r Al	a Se	er Va	l Gly 15
30	Asţ	Arg	Val	Thr 20		Thr	Cys	Arg		a Sei 25	Glr	s Se	r Il	.e Se	er Ar 30	g Trp
35	Lev	ı Ala	Trp 35		Gln	Gln	Lys		Gly 0	y Lys	val	l Pr	o Ly	s Le 45	eu Le	u Ile
	Tyz	Lys 50		Ser	Ser	Leu		ser 5	Gly	y Vai	l Pro	s Se	r Ar 60	g Pi	ne Se	r Gly
40	Sez 65		Ser	Gly	Thr	Glu 70		Thr	Le	u Thi	r Ile 75	e Se 5	r Se	er Le	eu Gl	n Pro _ 80
	Ası) Asp	Phe	Ala	Thr 85		Тух	Cys	Gli	n Gli	n Tyr 90	. As	n Se	er Ty	r Se	r Phe 95
45	Gly	y Pro	Gly	Thr 100		va:	l As	p Il	e Ly 10	ys Ai 05	rg Tì	ır				
50	(13) INF	ORMA	TION F	OR SE	Q ID I	NO:13										
	(i) S	SEQUE	NCE C	HARAG	CTERI	STICS	:									
55		(B) TY	NGTH: PE: am POLO	ino aci	d	cids										
	(ii) l	MOLEC	ULE T	YPE: p	eptide											

(xi) S	SEQUE	NCE [DESCRIP	TION:	SEQ II	D NO:13:
--------	-------	-------	---------	-------	--------	----------

5	Gln 1	Val	Gln	Leu	Gln 5		Ser	Gly	Thr		Leu 0	Ala	Arg	Pro	_	.Ala 15
10	Ser	· Val	Arg	Leu 20		Cys	Lys	Ala	Ser 2	_	Tyr	Thr	Phe		Thr 30	Phe
	Gly	lle	Thr 35	Trp	Val	Lys	Gln	Arg 40	_	Gly	Gln	Gly		Glu 5	Trp	Ile
-15	Gly	Glu 50		Phe	Pro	Gly	Asn 55		Lys	Thr	Tyr	-	Ala O	Glu	Arg	Phe
20	Lys 65	Gly	Lys	Ala	Thr	Leu 70	Thr	Ala	Asp	Lys	Ser 75	Ser	Thr	Thr	Ala	Tyr 80
	Met	Gln	Leu	Ser	Ser 85	Leu	Thr	Ser	Glu	Asp 9		Ala	Val	Tyr		Cys 5
25	Ala	Arg	Glu	Ile 100	Arg	ту г	Trp	Gly	÷							
30	(14) IN								•							
35		(B) T	ENGTI YPE: a	H: 107 amino a	amino acid											
	(ii)	MOLE	CULE	TYPE	: pepti	de					-					
40	(xi) SEQL	JENCE	DESC	CRIPT	ION: S	SEQ IC	NO:1	14:							
	Gln 1	Val	Gln	Leu	Lys 5	Glu	Ser	Gly	Pro	Gly 1		Val	Ala	Pro		Gln .5
45	Ser	Leu	Ser	Ile 20	Thr	Cys	Thr	Val	Ser 25		Phe	Ser	Leu		Gly 0	Tyr
50	Gly	Val	Asn 35	Trp	Val	Arg	Gln	Pro 40		Gly	Lys	Gly		Glu 5	Trp	Leu
	Gly	Met 50	Ile	Trp	Gly	Asp	Gly 55		Thr	Asp	Tyr		Ser O	Ala	Leu	Lys
55							•									

(ii) MOLECULE TYPE: peptide

	Ser 65	Arg	Leu	Ser	Ile	Ser :	Lys :	Asp /	Asn S	Ser 1	Lys S 75	er G	ln Va	l Ph	80 E Ten	
5	Lys	Met	Asn	Ser	Leu 1 85	His '	Thr i	Asp 1	Asp 1	90	Ala A	rg T	үг Ту	r Cy	s Ala 95	
10	Arg	Glu	Arg	Asp 100	Tyr	Arg	Leu	Asp	Tyr 105	Trp	Gly			٠		
	(15) INF	ORMA	TION F	OR SE	EQ ID 1	NO:15										
15	(i) S	SEQUE	NCE C	HARA	CTERI	STICS	•								•	
		(B) TY		nino ac		cids									• •	
20	(ii) l	MOLEC	ULE T	YPE: p	eptide											
	(xi)	SEQUI	ENCE	DESCF	RIPTIO	N: SE	N OI C	O:15:							•	
25	Val 1		Leu	Gln	Gln 5		Gly	Ala	Glu		ı Met 10	: Lys	Pro	Gly	Ala Sei 15	c
30	Val	Lys	Ile	Ser 20		Lys	Ala	Ser		Ту <u>т</u> :5	Thr	Phe	Ser		TYP Tr	Ç
35	Ile	Glu	Trp 35	Val	Lys	Gln	Arg		Gly O	His	Gly	Leu		Trp 5	Ile Gly	7
33	Glu	Ile 50	Lēu	Pro	Gly	Ser	Gly 5		Thr	Ası	Tyr		Glu 60	Arg	Phe Lys	;
40	Gly 65		Ala	Thr	Phe	Thr 70	Ala	Asp	Thr	Ser	Ser 75		Thr	Ala	Tyr Met 80	
45	Gln	Leu	Asn	Ser	Leu 85	Thr	Ser	Glu	Asp		Gly	Val	Tyr	Tyr	Cys Leu 95	Ł
	His	Gly	Asn	Tyr 100	Asp	Phe	Asp	Gly	7 Tr	_	Y					
50	(16) INF	ORMA	TION F	OR SE	Q ID N	NO:16							•	÷		
	(i) S	EQUE	NCE C	HARAG	CTERIS	STICS	;									
55		(A) LE (B) TY (C) TO	PE: an	ino aci	id	cids										

5	Asp 1	Val	Gln	Leu	Gln 5		Ser	Gly	Pro	Ser 1	_	Val	Lys	Pro		Gln L5
	Thr	Leu	Ser	Leu 20	Thr	Cys	Ser	Val	Thr		Asp	Ser	Ile	_	Ser 0	Asp
10	Tyr	Trp	Ser 35	Trp	Ile	Arg	Lys	Phe 40		Gly	Asn	Arg		Glu 5	Tyr	Met
. 15	Gly	Tyr 50	Val	Ser	Tyr	Ser	Gly 55	_	Thr	Tyr	Tyr	_	Pro O	Ser	Leu	Lys
20	Ser 65	Arg	Ile	Ser	Ile	Thr 70	Arg	Asp	Thr	Ser	Lys 75	Asn	Gln	Tyr	Tyr	Leu 80
	Asp	Leu	Asn	Ser	Val 85	Thr	Thr	Glu	Asp	Thr		Thr	Tyr	Tyr		Ala 95
25	Asn	Trp	Asp	Gly 100	Asp	Tyr	Trp	Gly	•			-				
·30	(17) IN (i)	FORM SEQU												,		
35		(B) T	ENGTI YPE: a	amino		acids	· · .									
•	(ii)	MOLE	CULE	TYPE	: pepti	de			•							
40	(xi	SEQI	JENCE	E DES	CRIPT	ION: S	SEQ IC	NO:1	7 :			· .				
	Glu 1	Val	Lys	Leu	Leu 5		Ser	Gly	Gly	Gly 1		Val	Gln	Pro		Gly L5
-45	Ser	Leu	Lys	Leu 20	Ser	Cys	Ala	Ala	Ser 25		Phe	Asp	Phe	Ser 3	Lys 0	Tyr
50	Trp	Met	Ser 35	Trp	Val	Arg	Gln	Ala 40		Gly	Lys	Gly	Leu 4		Trp	Ile
55	Gly	Glu 50	Ile	His	Pro	Asp	Ser 55		Thr	Ile	Asn		Thr O	Pro	Ser	Leu

	Lys 65	Asp	Lys	Phe	Ile :	Ile : 70	Ser A	Arg A	Asp A		la Ly 75	/S AS	n Se	r Le	u Tyr 80	
5	Leu	Gln	Met	Ser	Lys ' 85	Val 1	Arg S	Ser (Slu A	.sp Tl 90	nr Al	la Le	u Ty	гТу	r Cýs 95	5
10	Ala	Arg	Leu	His 100	Tyr	Tyr	Gly	Tyr	Asn 105	Ala 1	Cyr I	rp G	ly			
	(18) IN	FORM	ATION	FOR S	EQ ID	NO:18	3									
15	. (i)	SEQU	ENCE	CHARA	CTER	ISTICS	S:									
15		(B) T	ENGTH YPE: ai OPOLC	mino a	cid	acids										
20	· (ii)	MOLE	CULE	TYPE:	peptide	е .										
	(xi) SEQL	JENCE	DESC	RIPTIC	ON: SE	Q ID N	NO:18:								
25	Glu 1		Gln	Leu	Val	_	Ser	Gly	Gly		Val O	Val	Gln	Pro	Gly	Arg L5
30	Ser	Leu	Arg	Leu 20		Cys	Ser	Ser	-	Gly 5	Phe	Ile	Phe		Ser 30	Tyr
35	Ala	Met	Tyr 35	_	Val	Arg	Gln	_	Pro O	Gly	Lys	Gly	_	Glu 5	Trp	Val
	Ala	Ile 50		Trp	Asp	Asp	Gly 5	_	Asp	Gln	His		Ala O	Asp	Ser	Val
40	Lys 65	_	Arg	Phe	Thr	Ile 70		Arg	Asn	Asp	Ser 75	Lys	Asn	Thr	Leu	Phe 80
45	Leu	Gln	Met	Asp	Ser 85		Arg	Pro	Glu	Asp 9		Gly	Val	Tyr	Phe	Cys 5
	Ala	Arg	Asp	Gly 100		His	Gly	Phe	Cys 10		Ser	Ala	Ser	Cys 11	Phe .0	Gly
50 .	Pro	Asp	Tyr 115	Trp	Gly											
55	(19) IN	FORM	ATION	FOR S	EQ ID	NO:19)									
	(i)	SEQUI	ENCE (CHARA	ACTER	ISTICS	S:									

	. (8	3) TYP	E: am	113 an ino aci SY: line	d	cids										
5	(ii) M	OLECI	JLE T	YPE: p	eptide											
	(xi) S	EQUE	NCE [ESCR	RIPTIO	N: SE	QIDN	IO:19:								
10	Glu 1	Val	Lys	Leu	Val 5		Ser	Gly	Gly	Gly 1		Val	Gln	Pro		Gly 15
15	Ser	Leu	Arg	Leu 20	Ser	Cys	Ala	Thr	Ser 25		Phe	Thr	Phe	Ser 3	Asp 0	Phe
	Tyr	Met	Glu 35	Trp	Val.	Arg	Gln	Pro 40		Gly	Lys	.Arg		Glu 5	Trp	Ile
20	Ala	Ala 50	Ser	Arg	Asn	Lys	Gly 55		Lys	Tyr	Thr		Glu O	Tyr	Ser	Ala
25	65					70					75			Gln		80
	Leu	Tyr	Leu	Gln	Met 85		Ala	Leu	Arg	Ala 9		Asp	Thr	Ala		Tyr 5
30	Tyr	Cys	Ala	Arg 100	Asn	Tyr	Tyr	Gly	Ser 10	Thr 5	Trp	Tyr	Phe	Asp 11	Val .0	Trp
35	Gly	•					•							•		
ĺ	(20) INFC															
40	(,	A) LEN B) TYF	IGTH: PE: am	HARAO 107 ar iino aci 3Y: line	mino a id		5 :									
				YPE: p)										
45	(xi) S	EQUE	NCE [DESCF	RIPTIO	N: SE	Q ID N	10:20:								
50 ·	Val		Leu	Glu	Gln 5	Ser	Gly	Pro	Gly	Leu 1	Val O	Arg	Pro	Ser	Gln 1	Thr .5
	Leu	Ser	Leu	Thr 20		Thr	Val	Ser	Gly 2	Thr 5	Ser	Phe	Asp	Asp 3	Tyr O	Tyr

	Şer	Thr	Trp 35	Val	Arg	Gln	Pro	Pro 40	_	Arg	Gly	Leu		Trp 5	Ile	Gly
5	•															
J	Tyr	Val 50	Phe	Tyr.	His	Gly	Thr 55		Asp	Thr	Asp		Pro O	Leu	Arg	Ser
10	Arg 65	Val	Thr	Met	Leu	Val 70	Asn	Thr	Ser	Lys	Asn 75	Gln	Phe	Ser	Leu	Arg 80
	Leu	Ser	Ser	Val	Thr 85	Ala	Ala	Asp	Thr	Ala 9		Tyr	Tyr	Cys		Arg 95
15	Asn	Leu	Ile	Ala 100	Gly	Cys	Ile	Asp	Val 105		o Gly	. 7				
20	(21) INF	ORMA	ATION	FOR S	EQ ID	NO:2	1 ′									
20	(i) S	EQUE	NCE (HARA	CTER	RISTIC	S:									
25		(B) TY	NGTH PE: ai	mino a	cid	acids										
	(ii) l	MOLE	CULE .	TYPE:	peptid	е										
30	(xi)	SEQU	ENCE	DESC	RIPTI	ON: SI	EQ ID	NO:21	:							•
	Ġlu 1	Val	Lys	Leu	Asp 5	Glu	Thr	Gly	Gly	Gly 1		Val	Gļn	Pro	Gly 1	Arg .5
35	Pro	Met	Lys	Leu 20	Ser	Cys	Val	Ala	Ser 25		Phe	Thr	Phe	Ser 3	Asp O	Tyr
40	Trp	Met	Asn 35		Val	Arg	Gln	Ser 40	Pro	Glu	Lys	Gly	Leu 4	Glu 5	Trp	Val
	Ala	Gln 50	_Ile	Arg	Asn	Lys	Pro 55	Tyr	Asn	Туг	Glu	Thr 6	Tyr O	Tyr	Ser	Asp
45	Ser 65	Val	Lys	Gly	Arg	Phe 7.0	Thr	Ile	Ser	Arg	Asp 75	Asp	Ser	Lys	Ser	Ser 80
50	Val	Tyr	Leu	Gln	Met 85		Asn	Leu	Arg	Val 9	Glu O	Asp	Met	Gly	Ile	Tyr 5
	Tyr	Cya	Thr	Gly 100		Туг	туг	Gly	Met 105	. Ası	э Туг	r Tr	o Gl	Y		
55	(22) INF	FORM/	ATION	FOR S	SEQ ID	NO:2	2									
	(i) S	SEQUE	ENCE (CHARA	ACTEF	RISTIC	S:									

		(A) LE (B) TY (C) TO	PE: an	nino ad	cid	acids										
5	(ii) !	MOLEC	ULE T	YPE:	peptid	е										
	(xi)	SEQUI	ENCE	DESC	RIPTIO	ON: SE	EQ ID I	NO:22	•							
10	Gln 1	Val	Gln	Leu	Lys S		Ser	Gly	Ala	Glu 1		Val	Ala	Ala		Ser 15
15	Ser	Val	Lys	Met 20	Ser	Cys	Lys	Ala	Ser 2		Tyr	Thr	Phe	_	Ser 30	Туг
	Gly	. Val	Asn 35	Trp	Val	Lys	Gln	Arg 40	_	Gly	Gln	Gly	_	Glu 5	Trp	Ile
20	Gly	Tyr 50	Ile	Asn	Pro	Gly	Lys 55		Tyr	Leu	Ser		Asn 0	Glu	Lys	Phe
25	Lys 65	Gly	Lys	Thr	Thr	Leu 70	Thr	Val	Asp	Arg	Ser 75	Ser	Ser	Thr	Ala	Tyr 80
	Met	Gln	Leu	Arg	Ser 85	Leu	Thr	Ser	Glu	Asp 9	_	Ala	Val	Tyr		Cys 95
30	Ala	Arg	Ser	Phe 100	Tyr	Gly	Gly	Ser	Asp 10		Ala	Val	Tyr	Tyr 11		Asp
35	Ser	Trp	Gly 115								٠	•		•		
	(23) INF	ORMA	TION	FOR S	EQ ID	NO:2	3									
40	(i) S	SEQUE	NCE C	HARA	CTER	ISTIC	S:									
45		(A) LE (B) TY (C) TC	PE: ar	nino a	cid	acids				-						
40	(ii) I	MOLEC	CULE 1	YPE:	peptid	е										
	(xi)	SEQUI	ENCE	DESC	RIPTIO	ON: SE	EQ ID	NO:23	3 :							
50	Glu 1	Val	Gln	Leu	Gln 5	Gln	Ser	Gly	Val	Glu 1		Val	Arg	Ala	Gly 1	Ser 5
55	•															

	Ser	Val	Lys	Met 20	Ser	Cys	Lys	Ala	Ser 2		Tyr	Thr	Phe		Ser 30	Asn
5	Gly	Ile	Asn 35	Trp	Val	Lys	Gln	Arg 40		Gly	Gln	Gly		Glu 5	Trp	Ile
10	Gly	Tyr 50	Asn	Asn	Pro	Gly	Asn 55		Tyr	Ile	Ala		Asn O	Glu	Lys	Phe
	Lys 65	Gly	Lys	Thr	Thr	Leu 70	Thr	Val	Asp	Lys	Ser 75	Ser	Ser	Thr	Ala	Tyr 80
	Met	Gln	Leu	Arg	Ser 85	Leu	Thr	Ser	Glu	Asp 9		Ala	Val	Tyr	Phe 9	Cys 5
20	Ala	Arg	Ser	Glu 100	Tyr	Tyr	Gly	Gly	Ser 10		Lys	Phe	Asp	Tyr 11	Trp .0	Gly
•	(24) INF	FORM	ATION	FOR	SEQ II	D NO:	24									
25	(i) S	SEQUE	ENCE	CHAR	ACTE	RISTIC	CS:									
30		(B) T	YPE: a	H: 117 Imino a OGY: Ii	acid	acids									•	
	(ii)	MOLE	CULE	TYPE:	pepti	de										
	(xi)	SEQL	JENCE	DESC	CRIPT	ION: S	SEQ ID) NO:2	4:							
35	Glu 1	Val	Gln	Leu	Val 5		Ser	Gly	Gly	Gly 1		Val	Gln	Pro	Gly 1	Arg 5
40	Ser-	Leu	Arg	Leu 20	Ser	Cys	Ala	Ala	Ser 25	_	Phe	Thr	Phe	_	Asp 0	Tyr
45	Ala	Met ⁻	His 35	Trp	Val	Arg	Gln	Ala 40		Gly	Lys	Gly	Leu 4		Trp	Val
	Ser	Gly 50	Ile	Ser	Trp	Asp	Ser 55		Ser	Ile	Gly	Tyr 6	_	Asp	Ser '	Val
50	Lys 65	Gly	Arg	Phe	Thr	Ile 70	Ser	Arg	Asp	Asn	Ala 75	Lys	Asn	Ser	Leu '	Tyr 80
	Leu	Gln	Met	Asn	Ser 85	Leu	Arg	Ala	Glu	Asp 90		Ala	Leu	Tyr	Tyr 9	
55			•													

	100 105 110 The trip rap for the trip val A
5	Phe Asp Ile Trp Gly 115
10	(25) INFORMATION FOR SEQ ID NO:25
15	(i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 111 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:
	Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gl 1 5 10 15
25	Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ile Ile Ile His Se 20 25 30
30	Asp Gly Asn Thr Tyr Leu Glu Trp Phe Leu Gln Lys Pro Gly Gln Se 35 40 45
35	Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro 50 60
	Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Met Ile 65 70 75 8
40 -	Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gl 85 90 95
45	Ser His Val Pro His Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile 100 105 110
	(26) INFORMATION FOR SEQ ID NO:26
50	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 110 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
55	(ii) MOLECULE TYPE: peptide
	() SECUENCE RESCRIPTION: SEC ID NO.28.

. 5	, Gin	ser	val	Leu	The 5	GIR	PIO	Pro	ser	Ala 1		GIÅ	Thr	Pro	_	Gln 15
	Arg	Val	Thr	Ile 20	Ser	Cys	Ser	Gly	Thr 2		Ser	Asn	Ile	-	Ser 30	Ser
10	Thr	Val	Asn 35	Trp	Tyr	Gln	Gln	Leu 40		Gly	Met	Ala		Lys 5	Leu	Leu
15	Ile	Tyr 50	Arg	Asp	Ala	Met	Àrg 55		Ser	Gly	Val	_	Asp O	Arg	Phe	Ser
	Gly 65	Ser	Lys	Ser	Gly	Ala 70	Ser	Ala	Ser	Leu	Ala 75	Ile	Gly	Gly	Leu	Gln 80
20 .	Ser	Glu	Asp	Glu	Thr 85	Asp	Tyr	Tyr	Cys	Ala 90	_	Trp	Asp	Val	_	Leu 95
25	Asn	Ala	Tyr	Val 100	Phe	Gly	Thr	Gly	Thr 105		va]	Thi	Va.	Let 110		
	(27) INI	ORM	ATION	FOR S	SEQ II) NO:	27									
30	(i) S	SEQUE	ENÇE (CHAR.	ACTE	RISTIC	CS:									
		(B) T	ENGTH PE: a	mino a	ecid	acids										
35	(ii)	MOLE	CULE	TYPE:	: pepti	de					•					
	 (xi)	SEQU	IENCE	DESC	CRIPT	ION: S	SEQ ID	NO:2	7:				-			
40	Gln 1	Val	Leu	Met	Thr 5	Gln	Thr	Pro	Ser	Ser	_	Pro	Val	Thr		Gly .5
45	Gln	Gln	Ala	Ser 20	Ile	Ser	Суз	Arg	Ser 25		Gln	Ile	Ile	_	His O	Ser
40	Asp	Gly	Asn 35	Thr	Tyr	Leu	Glu	Trp		Leu	Gln	Lys	Pro 4		Gln	Ser
50	Pro	Lys 50	Leu	Leu	Ile	Tyr	Lys 55		Ser	Asn	Arg	Phe 6		Gly	Val	Pro
55	Asp 65	Arg	Phe	Ser	Gly	Ser 70	Gly	Ser	Gly	Thr	Ser 75	Phe	Thr	Leu	Ala	Ile 80

	Ser	Arg	Val	Glu	Ala 85	Glu	Asp	Glu	Gly	Val		Tyr	Cys	Phe		Gly 95
5	Ser	His	Val	Pro 100		Thr	Phe	e Gly	Gly 105		y Th	ŗ Ly	s Le	u Gl 11		.e
10	(28) INF															
	(1) \$	SEQUE	NCE	CHARA	ACIER	astic	S:									
15		(B) TY	'PE: aı	l: 112 a mino a)GY: lir		acids										
	(ii)	MOLE	CULE	TYPE:	peptid	е										
20	(xi)	SEQU	ENCE	DESC	RIPTIO	ON: SI	EQ ID	NO:28	3:							
	Asp 1	Val	Val	Met	Thr 5	Gln	Ser	Pro	Leu	Ser 10		Pro	Val	Thr		Gly .5
25	Gln	Pro	Ala	Ser 20	Ile	Ser	Cys	Arg	Ser 25		Gln	Ser	Leu	Val		Ser
30	Asp	Gly	Asn 35	Thr	Tyr	Leu	Asn	Trp 40		Gln	Gln	Arg		Gly 5	Gln :	Ser
35	Prọ.	Arg 50	Arg	Leu	Ile	Tyr	Lys 55		Ser	Asn	Arg	Asp 6	_	Gly	Va1	Pro
•	Asp 65	Arg	Phe	Ser	Gly	Ser 70	Gly	Ser	Gly '	Thr	Asp 75	Phe	Thr	Leu	Lys	Ile 80
40	Ser	Arg	Val	Glu	Ala 85	Glu	Asp	Val	Gly '	Val 90	_	Tyr	Cys	Met	_	Gly 5
45	Thr	His	Trp	Ser 100	Trp	Thr	Phe	Gly	Gln 105		Thr	Lys 	Val	Glu 11		Lys
	(29) INF	FORMA	ATION	FOR S	SEQ ID	NO:2	9									
	· (i) \$	SEQUE	NCE (CHARA	ACTER	RISTIC	S:									
50		(B) TY	PE: a	l: 111 a mino a)GY: lii		acids										
55	(ii)	MOLE	CULE .	TYPE:	peptid	е										
	/vi)	SEOU	ENCE	DESC	PIDTI	ON: SI		NO-20	١٠							

5	Asp 1	val	Leu	Met	Thr	Gln	Ser	Pro	Leu		Leu .0	Pro	Val	. Thr	Leu	ı Gly 15
	Gln	Pro	Ala	Ser 20		Ser	Cys	Arg	Ser 2	_	Gln	Ile	Ile		His 30	s Ser
10	Asp	Gly	Asn 35	Thr	Tyr	Leu	Glu	Trp		Gln	Gln	Arg		Gly 45	Gln	Ser
15	Pro	Arg 50	Leu	Leu	Ile	Tyr	Lys 55		Ser	Asn	Arg		Ser 0	Gly	Val	Pro
	Asp 65	Arg	Phe	ser	Gly	Ser 70	Gly	Ser	Gly	Thr	Asp 75	Phe	Thr	Leu	Lys	Ile 80
20	Ser	Arg	Val	Glu	Ala 85	Glu	Asp	Val	Gly	Val	_	Tyr	Cys	Phe		Gly 95
25	Ser	His	Val	Pro 100	His	Thr	Phe	Gly	Gly 105	_	/ Thi	r Ly:	s Vā	l Gl 11		.e
	(30) INF	ORMA	TION F	OR S	EQ ID	NO:30)									
30	(i) S	EQUE	NCE C	HARA	CTER	ISTICS	S:									
		(A) LE (B) TY (C) TO	PE: an	nino ac	id	icids								·		
35 .	(ii) f	MOLEC	ULE T	YPE: p	peptide	Э										
	(xi)	SEQUE	ENCE	DESC	RIPTIC	ON: SE	(Q ID 1	10:30	:							
40	Asp . 1	Ile	Val	Met	Thr 5	Gln	Ser	Pro	Asp	Ser 10	_	Ala	Val	Ser		Gly .5
45	Glu	Arg_	Ala	Thr 20	Ile	Asn	Cys	Lys	Ser 25		Gln	Ser	Val		Tyr O	Ser
	Ser	Asn	Asn 35	Lys	Asn	Tyr	Leu	Ala 40	_	Tyr	Gln	Gln		Pro 5	Gly	Gln
50	Pro	Pro 50	Lys	Leu	Leu	Ile	Tyr 55		Ala	Ser	Thr	Arg 60		Ser	Gly	Val
55	Pro 65	Asp	Arg	Phe	Ser	Gly 70	Ser	Gly	Ser	Gly	Thr 75	Asp	Phe	Thr	Leu	Thr 80

	Ile	Ser	Ser	Leu	Gln 85	Ala	Glu	Asp	Val	Ala 9	Val 0	Tyr	Tyr	Cys	Glr	ı Gln 95
5	Tyr	Asp	Thr	Ile 100	Pro	Thr	Phe	Gly	Gly 10		Thr	Lys	Val		Ile 10	Lys
10	(31) IN	FORM	ATION	FOR:	SEQ IE	O NO:3	31						•			
	(i)	SEQU	ENCE	CHAR	ACTE	RISTIC	CS:									
15	,	(B) T	ENGTI YPE: a	mino a	acid	acids										
	(ii)	MOLE	CULE	TYPE	: peptio	de										
20	(xi) SEQI	JENCE	DES	CRIPTI	ION: S	EQ ID	NO:31	l :							
25	Asp	Val	Leu	Met	Thr 5	Gln	Thr	Pro	Asp	Ser 1		Pro	Val	Ser		Gly L5
•	Asp	Arg	Ala	Ser 20	Ile	Ser	Cys	Arg	Ser 25	_	Gln	Ile	Ile	_	His O	Ser
30	Asp	Gly	Asn 35	Thr	Tyr	Leu	Glu	Trp		Leu	Gln	Lys		Gly 5	Gln	Ser
35	Pro	Lys 50	Leu	Leu	Ile	Tyr	Lys 55		Ser	Asn	Arg	Phe 6	_	Gly	Val	Pro
40	Asp 65	Arg	Phe	Ser	Gly	Ser 70	Gly	Ser	Gly	Thr	Asp 75	Phe '	Thr	Leu	Met	Ile 80
	Ser	Arg	Val	Glu	Ala 85	Glu	Asp	Leu	Gly	Val 90	TYT	Tyr	Cys	Phe	_	Gly 5
45	Ser	His	Val	Pro 100	His	Thr	Phe	Gly	Gly 105		Thr	Lys	. Leu	110		2
	(32) IN	IFORM	ATION	FOR	SEQ II):ON C	32									
50	(i)	SEQU	ENCE	CHAR	ACTE	RISTIC	CS:									-*
55		(B) T	ENGTI YPE: a	amino a	acid	acids										
	(ii)	MOLE														
	/:	VCEOL	TENOR			ONL C	EO ID	AIC.22	3.							

	Asp 1	Val	Gln	Leu	Val 5	Gĺu	Ser	Gly	Gly	Gly 10	_	Val	Gln	Pro		Gly .5
5	Ser	Arg	Lys	Leu 20	Ser	Cys	Ala	Ala	Ser 25		Phe	Thr	Phe	_	Ser O	Phe
10	Gly	Met	His 35	Trp	Val	Arg	Gln	Ala 40		Glu	Lys	Gly	_	Glu 5	Trp	Val
15	Ala	Tyr 50	Ile	Ser	Ser	Gly	Ser 55		Thr	Ile	Tyr		Ala O	Asp	Thr	Val
	Lys 65	Gly	Arg	Phe	Thr	Ile 70	Ser	Arg	Asp	Asn	Pro 75	Lys	Asn	Thr	Leu	Phe 80
	Leu	GÌn	Met	Thr	Ser 85	Leu	Arg	Ser	Glu	Asp 90		Ala	Met	Tyr		Cys 5
25	Ala	Arg	Met	Arg 100	Lys	Gly	Tyr	Ala	Met 10		Tyr	Trp	Gly	Gln 11		Thr
. •	Ťhr	Val	Thr 115	Val	Ser						٠					
30	(33) II	NFORM	OITAN	1 FOR	SEQ II	D NO:	33		•							
	(i)	SEQL	JENCE	CHAF	RACTE	RISTI	CS:							•		
35		(B)	ENGT TYPE: a	amino	acid	acids			٠							
40	(ii) MOL	ECÚLE	TYPE	: pepti	de										
,	(x	i) SEQ	UENCI	E DES	CRIPT	ION: S	SEQ IC	NO:3	3:							
4 5	Glu 1	Val.	_GIn_	Leu	Val 5		Ser	Gly	Gly	Gly 1		Val	Gln	Pro	Gly	Arg LS
	Ser	Leu	Arg	Leu 20		Cys	Ser	Ser	Ser 2		Phe	Ile	Phe	Ser 3	Ser 0	Tyr
50	Ala	Met	Tyr 35	Trp	Val	Arg	Gln	Ala 40	Pro O	Gly	Lys	Gly	Leu 4	Glu IS	Trp	Val
55	Ala	Ile 50	Ile	Trp	Asp	Asp	Gly 5		Asp	Gln	Ris	Tyr	Ala 0	Asp	Ser	Val

	Lys 65	Gly	Arg	Phe	Thr	Ile 70	Ser	Arg	Asn	Asp	Ser 75	Lys	Asn	Thr	Leu	Phe 80
5	Leu	Gln	Met	Asp	Ser 85		Arg	Pro	Glu	Asp 9		Gly	Val	Tyr		Cys 95
10	Ala	Arg	Asp	Gly 100	Gly	His	Gly	Phe	Cys 105		Ser	Ala	Ser	Cys 11		Gly
٠	Pro	Asp	Tyr 115	Trp	Gly	Gln	Gly	Thr 120		Va.	l Thi	Va:	1 Se:			
15	(34) INF	ORMA	TION F	OR SE	EQ ID I	NO:34										
	(i) S	EQUE	NCE C	HARA	CTERI	STICS	; :									
20	-	(A) LEI (B) TYI (C) TO	PE: am	ino ac	id	cids										
?5	(ii) N	MOLEC	ULE T	YPE: p	eptide	•										
0	(xi)	SEQUE	NCE [DESCF	RIPTIO	N: SE	Q ID N	10:34:								
30	Glu 1	Val	Gln'	Leu	Val 5		Ser	Gly	Gly	Gly 1	_	Val	Gln	Pro	_	Arg .5
35	Ser	Leu	Arg	Leu 20	Ser	Cys	Ala	Ala	Ser 25		Phe	Ile	Phe		Ser O	Phe
	Gly	Met	His 35	Trp	Val	Arg	.Gln	Ala 40		Gly	Lys	Gly		Glu 5	Trp	Val
10		Tyr 50	Ile	Ser	Ser	Asp	Gly 55		Thr	Ile	Tyr	His 6		Asp	Ser	Val
1 5	Lys 65	Gly_	_Arq	Phe	Thr	Ile 70	Ser	Arg	Asp	Asp	Pro 75	Lys	Asn	Thr	Leu	Phe 80
	Leu	Gln	Met	Thr	Ser 85	Leu	Arg	Ser	Glu	Asp 90		Ala	Met	Tyr		Cys 5
50	Ala	Arg	Met	Arg 100	Lys _.	Gly	Tyr	Ala	Met 105		Tyr	Trp	Gly	Gln 11	Gly 0	Thr
55	Thr	Val	Thr 115	Val	Ser											
	(35) INF	ORMA	TION F	OR SE	EQ ID	NO:35										

(i) SEQUENCE CHARACTERISTICS:

			NGTH			acids										
5		(C) TO	OPOLO)GY: lir	near											
	(ii) 1	MOLE	CULE .	TYPE:	peptid	le										
10	(xi)	SEQU	ENCE	DESC	RIPTI	ON: S	EQ ID	NO:3	5:							
	Gln 1	Val	Gln	Leu	Val 5		Ser	Gly	Gly	_	Val 0 -	Val	Gln	Pro	Gly	Arg L5
15	Ser	Leu	Arg	Leu -20	Ser	Cys	Ala	Ala	Ser 29		Phe	Thr	Phe		Ser 10	Tyr
20	Ala	Met	His 35	Trp	Val	Arg	Gln	Ala 40		Gly	Lys	Gly		Glu 5	Trp	Val
25	Ala	Val 50	Ile	Ser	Tyr	Asp	Gly 55		Asn	Lys	Tyr		Ala O	Asp	Ser	Val
	Lys 65	Gly	Arg	Phė	Thr	Ile 70	Ser	Arg	Asp	Asn	Ser 75	Lys	Asn	Thr	Leu	Tyr 80
30	Leu	Gln	Met	Asn	Ser 85		Arg	Ala	Glu	Asp 9		Ala	Val	Tyr	Tyr	Cys 5
35	· Ala	_	Asp	Arg 100		Asp	Trp	Gly	Trp 10		Leu	Phe	Asp	Tyr . 11	Trp .0	Gly
	Gln	Gly	Thr 115	Leu	Val	Thr	Val	. Ser								
40	(36)	INF	ORMA	TION	FOR	SEQ	ID	NO:3	6							
	(i) S	SEQUE	ENCE (CHARA	ACTE	RISTIC	S:									
45		(B) T	ENGTH (PE: at OPOLO	mino a	cid	acids				t						
	(ii)	MOLE	CULE	TYPE:	peptic	de										
50	(xi)	SEQU	ENCE	DESC	RIPTI	ON: S	EQ ID	NO:36	6:							
55	Gln 1	Val	Gln	Leu	Val 5		Ser	Gly	Gly	Gly 1		Val	Gln	Pro	Gly 1	Arg .5

	Ser	Leu	Arg	Leu 20	Ser	Cys	Ala	Ala	Ser 25		Phe	Thr	Phe		Ser 0	Phe
5	Gly	Met	His 35	Trp	Val	Arg	Gln	Ala 40		Gly	Lys	Gly	Leu 4		Trp	Val
10	Ala	Tyr 50	Ile	Ser	Ser	Gly	Ser 55		Thr	Ile	Tyr	Tyr 6		Asp	Ser	Val
15	Lys 65	Gly	Arg	Phe	Thr	Ile 70	Ser	Arg	Asp	Asn	Ser 75	Lys	Asn	Thr	Leu	Tyr 80
10	Leu	Gln	Met	Asn	Ser 85		Arg	Ala	Glu	Asp 9		Ala	Val	Tyr	Tyr 9	Cys 5
20	Ala	Arg		Arg 100	Lys	Gly	Tyr	Ala	Met 105		Tyr	Trp	GİY	Gln 11	Gly 0	Thr
25	Leu	Val	Thr 115	Val	Ser				٠.							
	(37) INF	ORMA	ATION	FOR S	EQ ID	NO:3	7									
	(i) S	SEQUE	NCE (CHARA	CTER	RISTIC	S:									
30		(B) TY	NGTH PE: ar	mino a	cid	cids										
35		MOLEG				e ON: SE	 -0 ID I	 NO:37								
								•								
40		Val	Gln	Leu	Val		Ser	Gly	Gly	Gly 1	Leu .0	Val	. Gln	Pro	Gly	Gly 15
	Ser	Leu	_yrd	Leu 20	Ser	Суз	Ala	Ala	Ser 2	Gly 5	Phe	Thr	Phe	Ser	Ser 30	Tyr
45	Trp	Met	Ser 35		Val	Arg	Gln	Ala 4	Pro 0	Gly	Lys	Gly	Leu	Glu 45	Trp	Val
50	Ala	Asn 50		Lys	Gln	Asp	Gly 5	Ser 5	Glu	Lya	Tyr	Tyr	Val	Asp	Ser	Val
55	Lys 65		Arg	Phe	Thr	Ile 70	Ser	Arg	Asp	Asn	Ala 75	Lys	. Asn	Ser	Leu	Tyr 80

	Ted Gill	nec asn	85	ALG ALG	9 grd Asp		var lår	95
5	Ala Arg					-		
10	(38) INFORMAT	TION FOR SI	EQ ID NO:3	8		,	. •	
	(i) SEQUEN	ICE CHARA	CTERISTIC	S:				•
15	(B) TYP	NGTH: 117 a PE: amino ad POLOGY: lin	cid					
	(ii) MOLEC	ULE TYPE: p	peptide	•				
20	(xi) SEQUE	NCE DESCI	RIPTION: SI	EQ ID NO:3	8:			
	Glu Val	Gln Leu	Val Glu 5	Ser Gly	Gly Gly		Gln Pro	Gly Gly 15
25	Ser Leu	Arg Leu 20	Ser Cys	Ala Ala	Ser Gly 25	Phe Thr	Phe Ser	
30	Gly Met	His Trp	Val Arg	Gln Ala	Pro Gly	Lys Gly	Leu Glu 9	Trp Val
	•				•			
	Ala Tyr 50	Ile Ser	Ser Gly	Ser Phe	Thr Ile	Tyr His		Ser Val
35	Lys Gly : 65	Arg Phe	Thr Ile	Ser Arg	Asp Asn	Ala Lys 75	Asn Thr	Leu Phe 80
40	Leu Gln	Met Thr	Ser Leu 85	Arg Ala	Glu Asp 90		Met Tyr	Tyr Cys 95
	Ala Argj	Met Arg 100	Lys Gly	Tyr Ala	Met Asp 105	Tyr Trp	Gly Gln (Sly Thr
45 .	Thr Val	Thr Val	Ser					
	(39) INFORMAT	TION FOR S	EQ ID NO:3	9				
· <i>50</i>	(i) SEQUEN	NCE CHARA	CTERISTIC	S:				
55	(B) TYF	NGTH: 15 an PE: amino ao POLOGY: lin	cid					
	(E) MOLECI	III E TVDE						

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

5	Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr 1 5 10 15
	(40) INFORMATION FOR SEQ ID NO:40
10	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:
· 20	
-	Lys Thr Ser Leu Arg Pro Gly Lys Gly Ser Ser Asp Tyr Glu Lys Lys 1 10 15
25	(41) INFORMATION FOR SEQ ID NO:41
	(i) SEQUENCE CHARACTERISTICS:
30	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
35	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:
	Lys Thr Ser Leu Arg Pro Gly Lys Gly Ser Ser Glu Tyr Glu Lys Lys 1 5 10 15
40	
	(42) INFORMATION FOR SEQ ID NO:42
45	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
50	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:
55	Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp His Glu Lys Lys 1 5 10 15

(43) INFORMATION FOR SEQ ID NO:43

	(i) SEQUENCE CHARACTERISTICS:
5	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:
15	Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Gln Glu Lys Lys 1 5 10 15
	(44) INFORMATION FOR SEQ ID NO:44
20	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:
30	Gln Ser Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Gln Glu Lys Lys 1 5 10 15
35	(45) INFORMATION FOR SEQ ID NO:45
	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:
. ús	Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Pro Glu Lys Lys 1 5 10 15
50	
	(46) INFORMATION FOR SEQ ID NO:46
55	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:46: 5 Gin Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Pro Glx Lys Lys (47) INFORMATION FOR SEQ ID NO:47 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 15 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:47: 20 Pro Asp Lys Gly Ser Ser Asp Pro Glu Lys Thr (48) INFORMATION FOR SEQ ID NO:48 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 30 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:48: Gln Thr Ser Leu Arg Ala Asp Lys Gly Ser Ser Asp Gln Glu Lys Lys 40 (49) INFORMATION FOR SEQ ID NO:49 (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:49: 55

(50) INFORMATION FOR SEQ ID NO:50

(i) SEQUENCE CHARACTERISTICS:

	•
5	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	∼ (ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:
	Gln Thr Ser Leu Arg Pro Ala Arg Gly Ser Ser Asp Gln Glu Lys Lys 1 5 10 15
15	
	(51) INFORMATION FOR SEQ ID NO:51
20	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:
30	Gln Thr Ser Leu Lys Pro Gly Arg Gly Ser Ser Asp Pro Glu Lys Lys 1 10 15
35	(52) INFORMATION FOR SEQ ID NO:52
	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:
	Gln Thr Ser Leu Arg Pro Gly Arg Gly Ser Ser Asp Thr Glu Lys Lys 1 5 10 15
50 .	(53) INFORMATION FOR SEQ ID NO:53
	(i) SEQUENCE CHARACTERISTICS:
55 ·	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

Gln Ile_Ser_Leu Arg Pro Gly Lys Gly Ser Ser Asp Ser Glu Lys Lys
1 10 15

(54) INFORMATION FOR SEQ ID NO:54

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLÓGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:
- Gln Thr Ser Leu Arg Pro Gly Lys Gly Asp Ser Asp Glu Asp Lys Lys
 1 5 10 15
 - (55) INFORMATION FOR SEQ ID NO:55
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:
 - Glu Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Ala Asp Lys Lys
 1 10 15
- (56) INFORMATION FOR SEQ ID NO:56
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:
- Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Glu Asp Lys Lys
 55 10 15
 - (57) INFORMATION FOR SEQ ID NO:57

	(i) SEQUENCE CHARACTERISTICS:
5	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:
	Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Glu Glu Lys Lys 1 5 10 15
15	
	(58) INFORMATION FOR SEQ ID NO:58
•	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids
	(B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:
30	Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asx Ala Asx Lys Lys 1 10 15
	(59) INFORMATION FOR SEQ ID NO:59
35	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(0)
	(ii) MOLECULE TYPE: peptide
	(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59: Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Glu Asp Asp Glu
45 50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59: Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Glu Asp Asp Glu 1 5 10 15
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59: Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Glu Asp Asp Glu 1 5 10 15 (60) INFORMATION FOR SEQ ID NO:60

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Gln Glu Thr Thr 1 5 10 15

(61) INFORMATION FOR SEQ ID NO:61

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide .
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:
- 20 Gln Asn Ser Leu Thr Pro Gly Lys Gly Ser Ser Pro Glu Lys Lys 1 5 10 15
 - (62) INFORMATION FOR SEQ ID NO:62
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:
 - Val Thr Lys Val Arg Pro Gly Lys Gly Asp Ser Asp Lys Lys 15
- 40 (63) INFORMATION FOR SEQ ID NO:63
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:
 - Val Thr Lys Val Arg Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
 1 10 15
 - (64) INFORMATION FOR SEQ ID NO:64
 - (i) SEQUENCE CHARACTERISTICS:

	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:
10	Val Thr Arg Val Arg Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 10 15
	(65) INFORMATION FOR SEQ ID NO:65
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:
25	Leu Thr Lys Val Arg Pro Gly Lys Gly Asp Ser Asp Ser Glu Lys Lys 1 10 15
30	(66) INFORMATION FOR SEQ ID NO:66
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:
45	Val Thr Lys Val Arg Pro Gly Lys Gly Asp Ser Asp Ser Glu Gln Lys 1 5 10 15
	(67) INFORMATION FOR SEQ ID NO:67
50	(i) SEQUENCE CHARACTERISTICS:
•	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
55	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

Val Thr Lys Val Arg Pro Glu Lys Gly Asp Ser Asp Ala Glu Lys Lys

(68) INFORMATION FOR SEQ ID NO:68 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 10 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:68: 15 Val Thr Lys Val Arg Pro Glu Lys Gly Asp Ser Asp Ser Glu Lys Lys 20 (69) INFORMATION FOR SEQ ID NO:69 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 30 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:69: 35 Val Thr Lys Val Ser Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys (70) INFORMATION FOR SEQ ID NO:70 40 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 45 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:70: 50 Val Thr Lys Val Arg Ser Gly Lys Gly Glu Ser Asp Ala Glu Lys Lys 55 (71) INFORMATION FOR SEQ ID NO:71 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear

5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:
10	Val Thr Ser Val Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
	(72) INFORMATION FOR SEQ ID NO:72
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:
25	Val Ser Ser Val Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
30	(73) INFORMATION FOR SEQ ID NO:73
11	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:
	Val Thr Ser Ala Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
45	(74) INFORMATION FOR SEQ ID NO:74
	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
55	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

	Val Ser Ser Ala Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 10 15
5	(75) INFORMATION FOR SEQ ID NO:75
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:
20	Val Thr Ser Ala Arg Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
	(76) INFORMATION FOR SEQ ID NO:76
25	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:
35	Val Ser Pro Ala Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
<u>.</u>	(77) INFORMATION FOR SEQ ID NO:77
40	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:
	Val Thr Lys Ala Arg Pro Gly Lys Gly Asp Ser Asp Val Glu Lys Asn 1 10 15
55	(78) INFORMATION FOR SEQ ID NO:78
	(i) SEQUENCE CHARACTERISTICS:

	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
5	(ii) MOLECULE TYPE: peptide	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:	
10	Val Thr Leu Ile Pro Pro Gly Lys Gly Asp Ser Asp Ala Glu	Lys Lys 15
	(79) INFORMATION FOR SEQ ID NO:79	
15	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear	
20	(ii) MOLECULE TYPE: peptide	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:	
25	Vai Thr Leu Leu Gln Pro Gly Lys Gly Asp Ser Asp Ala Glu I	ys Lys 15
	(80) INFORMATION FOR SEQ ID NO:80	•
30	(i) SEQUENCE CHARACTERISTICS:	
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:	
	Val Thr Leu Leu Gln Pro Gly Lys Gly Asp Ser Asp Ala Asp L 1 5 10	ys Lys 15
45	(81) INFORMATION FOR SEQ ID NO:81	
	(i) SEQUENCE CHARACTERISTICS:	
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:	

	1 5 10 15
5	(82) INFORMATION FOR SEQ ID NO:82
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
15	(ii) MOLECULE TYPE: peptide
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:
20	Val Thr Leu Leu Glm Ala Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
	(83) INFORMATION FOR SEQ ID NO:83
25	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
35	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:
	Val Thr Leu Leu Gln Pro Gly Glu Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
40	(84) INFORMATION FOR SEQ ID NO:84
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:
55	Leu Thr Leu Leu Gln Pro Gly Asn Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
	(85) INFORMATION FOR SEQ ID NO:85

(i) SEQUENCE CHARACTERISTICS:

	(A) LENGTH: 16 amino acids (B) TYPE: amino acid
5	(C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:
	Val Thr Leu Leu Gln Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Ile 1 5 10 15
15	(86) INFORMATION FOR SEQ ID NO:86
	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:
30 .	Val Thr Leu Phe Gln Pro Gly Gln Gly Asp Ser Asp Pro Glu Lys Lys 1 5 10 15
	(87) INFORMATION FOR SEQ ID NO:87
35	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:
45	Val Thr Leu Pro Gln Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
50	(88) INFORMATION FOR SEQ ID NO:88
50	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid
55	(C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

Val Thr Leu Pro Gln Pro Gly Lys Gly Asp Trp Asp Ala Glu Lys Lys
1 10 15

- (89) INFORMATION FOR SEQ ID NO:89
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid

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- (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

Val Thr Phe Leu Ser Pro Gly Gln Gly Asp Ser Asp Ala Glu Lys Lys
1 10 15

- (90) INFORMATION FOR SEQ ID NO:90
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

Glu Ser Ser Ala Arg Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 10 15

- (91) INFORMATION FOR SEQ ID NO:91
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:
- Val Thr Leu Ser Ser Pro Gly Gln Gly Asp Ser Asp Ala Glu Lys Lys
 1 10 15

(92) INFORMATION FOR SEQ ID NO:92

(i) SEQUENCE CHARACTERISTICS: 5 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:92: Val Thr Thr Ala Lys Pro Glu Lys Gly Asp Ser Asp Val Glu Lys Lys (93) INFORMATION FOR SEQ ID NO:93 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:93: 30 Val Thr Thr Pro Lys Pro Asp Lys Gly Asp Ser Asp Val Glu Lys Lys (94) INFORMATION FOR SEQ ID NO:94 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 40 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:94: 45 Val Thr Ala Pro Arg Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 15 50 (95) INFORMATION FOR SEQ ID NO:95 (i) SEQUENCE CHARACTERISTICS: 55 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:
5	Val Thr Ala Pro Lys Pro Gly Lys Gly Thr Ser Ser Ala Glu Lys Lys 1 5 10 15
10	(96) INFORMATION FOR SEQ ID NO:96
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:
25	Val Thr Thr Pro Lys Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 1 5 10 15
	(97) INFORMATION FOR SEQ ID NO:97
30	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
35	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:
40	Val Ser Ala Pro Lys Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 1 5 10 15
45	(98) INFORMATION FOR SEQ ID NO:98
45	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid
50_	(C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

Val Thr_Ala Pro Arg Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 1 10 15

(99) INFORMATION FOR SEQ ID NO:99 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 10 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:99: Val Thr Ala Pro Lys Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 20 (100) INFORMATION FOR SEQ ID NO:100 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 30 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:100: Val Thr Ala Pro Lys Pro Asp Lys Gly Val Ser Ser Ala Glu Lys Lys 35 (101) INFORMATION FOR SEQ ID NO:101 40 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 45 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:101: 50 Val Thr Ala Pro Lys Ser Glu Lys Gly Val Ser Ser Ala Glu Lys Lys (102) INFORMATION FOR SEQ ID NO:102 55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear

5 (ii) _MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:102: Phe Thr Ala Pro Lys Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 10 (103) INFORMATION FOR SEQ ID NO:103 (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:103: 25 Leu Thr Ala Pro Lys Pro Gly Arg Gly Val Ser Ser Ala Glu Lys Lys 30 (104) INFORMATION FOR SEQ ID NO:104 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 35 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:104: 40 Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Arg 45 (105) INFORMATION FOR SEQ ID NO:105 (i) SEQUENCE CHARACTERISTICS: 50 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

Val Ser Ala Pro Lys Pro Gly Lys Glu Gly Ser Ser Ala Glu Lys Lys 1 10 15

(106) INFORMATION FOR SEQ ID NO:106

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:
- Val Thr Ala Pro Lys Pro Arg Lys Gly Ala Ser Ser Ala Glu Lys Lys

 1 10 15
 - (107) INFORMATION FOR SEQ ID NO:107
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:
 - Val Thr Phe Leu Ser Pro Gly Gln Gly Asn Ser Asp Ala Glu Leu Pro
 - (108) INFORMATION FOR SEQ ID NO:108
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:
 - Val Thr Phe Leu Ser Pro Gly Gln Gly Asn Ser Asp Glu Asp Leu Pro 1 10 15
- 55 (109) INFORMATION FOR SEQ ID NO:109
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids (B) TYPE: amino acid

	(C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
•	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:
10	Val Thr Leu Ser Ser Pro Gln Arg Gly Asp Ser Asp Ala Glu Lys Lys 1 5 10 15
15	(110) INFORMATION FOR SEQ ID NO:110 (i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:
30	Val Thr Ala Pro Lys Ser Ser Lys Gly Gly Ser Ser Ala Glu Lys Lys 1 10 15 (111) INFORMATION FOR SEQ ID NO:111
35	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:
45	Gln Thr Ser Pro Thr Pro Gly Lys Gly Ser Ser Asp Pro Glu Lys Lys 1 5 10 15
	(112) INFORMATION FOR SEQ ID NO:112
50	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:112:

	1 5 10 15
5	(113) INFORMATION FOR SEQ ID NO:113
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
15	(ii) MOLECULE TYPE: peptide
,,,	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:113:
20	Val Thr_Ala Leu Lys Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys 1 10 15
	(114) INFORMATION FOR SEQ ID NO:114
	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:114:
35	Val Thr Ala Leu Lys Ser Asp Lys Gly Ala Ser Ser Gly Glu Lys Lys 1 5 10 15
	(115) INFORMATION FOR SEQ ID NO:115
40	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:115:
	Val Thr Pro Pro Ser Pro Gly Gln Gly Asp Ser Ala Ala Glu Lys Lys 1 5 10 15
55	(116) INFORMATION FOR SEQ ID NO:116
	(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear 5 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:116: Val Thr Pro Pro Ser Pro Gly Gln Gly Asp Ser Ala Arg Glu Lys Lys 10 (117) INFORMATION FOR SEQ ID NO:117 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:117: 25 Val Thr Val Arg Lys Pro Gly Lys Gly Asp Ser Ser Asp Glu Lys Lys (118) INFORMATION FOR SEQ ID NO:118 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 35 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:118: Gln Thr Ser Val Arg Leu Gly Gln Gly Ser Ser Asp Pro Glu Lys Lys 45 (119) INFORMATION FOR SEQ ID NO:119 (i) SEQUENCE CHARACTERISTICS: 50 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:

Lys Thr Ser Leu Arg Pro Trp Lys Gly Ser Ser Asp Ser Asp Lys Lys 1 5 10 15

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5 .	(120) INFORMATION FOR SEQ ID NO:120
•	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:
20	Gln Thr Asp Val Thr Gln Gly Gln Gly Ser Ser Gln Pro Glu Lys Lys 1 5 10 15
	(121) INFORMATION FOR SEQ ID NO:121
25	(i) SEQUENCE CHARACTERISTICS:
. '	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:
35	Gln Thr Ala Val Ser Gln Gly Gln Gly Ser Ser Gln Ser Glu Lys Lys 1 5 10 15
	(122) INFORMATION FOR SEQ ID NO:122
40	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:
50	Leu Thr Ala Pro Arg Thr Asn Arg Gly Ser Ser Asp Ser Glu Lys Lys 1 10 15
55	(123) INFORMATION FOR SEQ ID NO:123
35	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:123: Val Thr Ala Pro Ser Ser His Arg Gly Ser Ser Asp Thr Glu Lys Lys 5 10 10 (124) INFORMATION FOR SEQ ID NO:124 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:124: ²5 Leu Leu Ser Leu Ser Pro Leu Lys Gly Asp Ser Asp Pro Glu Lys Val (125) INFORMATION FOR SEQ ID NO:125 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 35 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:125: 40 Val Thr Ala Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Lys Leu 45 (126) INFORMATION FOR SEQ ID NO:126 50 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 55 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:126:

Val Thr Ile Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Lys Leu 1 5 10 15

5 .	(127) INFORMATION FOR SEQ ID NO:127
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:127:
20	Ala Val Ser Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Lys Leu 1 5 10 15 (128) INFORMATION FOR SEQ ID NO:128
	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
•	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:128:
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35	Ala Val Ser Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Lys Leu 1 10 15
35	
	1 - 5 10 15
35	1 - 5 10 15 (129) INFORMATION FOR SEQ ID NO:129
	1 - 5 10 15 (129) INFORMATION FOR SEQ ID NO:129 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid
40	(129) INFORMATION FOR SEQ ID NO:129 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(129) INFORMATION FOR SEQ ID NO:129 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide
40 45	(129) INFORMATION FOR SEQ ID NO:129 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:129: Ala Val Ser Pro Thr Pro Asp Thr Gly Val Ile Lys Thr Glu Lys Leu
40 45	(129) INFORMATION FOR SEQ ID NO:129 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:129: Ala Val Ser Pro Thr Pro Asp Thr Gly Val Ile Lys Thr Glu Lys Leu 1 5
40 45 50	(129) INFORMATION FOR SEQ ID NO:129 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:129: Ala Val Ser Pro Thr Pro Asp Thr Gly Val IIe Lys Thr Glu Lys Leu 1 5 10 (130) INFORMATION FOR SEQ ID NO:130

(C) TOPOLOGY: linear

	(ii) MOLECULE TYPE: peptide
5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:
	Ala Val Ser Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Pro Se 1 5 10 15
10	(131) INFORMATION FOR SEQ ID NO:131
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:
25	Tyr Leu Pro Pro Thr Pro Gly Val Ile Arg Ser Thr Ala Met Lys Leu 1 5 10 15
	(132) INFORMATION FOR SEQ ID NO:132
30	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
35	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:
40	Tyr Leu Pro Pro Thr Pro Gly Val Ile Arg Ser Thr Ala Met Arg Leu 1 5 10 15
45	(133) INFORMATION FOR SEQ ID NO:133
45	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:

	Tyr Leu Pro Pro Thr Pro Gly Leu Ile Arg Ser Thr Ser Met Lys Leu 1 5 10 15
5	(134) INFORMATION FOR SEQ ID NO:134
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
15	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134:
20	Tyr Leu Pro Pro Thr Pro Gly Leu Ile Arg Ser Thr Ser Val Lys Leu 1 5 10 15
	(135) INFORMATION FOR SEQ ID NO:135
25	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:
35 .	Tyr Leu Pro Pro Thr Pro Gly Val Ile Arg Ser Thr Ala Glu Lys Leu 1 5 10 15
40	(136) INFORMATION FOR SEQ ID NO:136
40	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:
	Tyr Leu Pro Pro Thr Pro Gly Val Ile Arg Ser Thr Ala Gly Lys Leu 1 10 15
55	(137) INFORMATION FOR SEQ ID NO:137
	(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids (B) TYPE: amino acid

	(C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:
10	Tyr Leu Pro Ala Thr Pro Gly Val Val Arg Ser Ser Ala Gly Met Leu 1 10 15
	(138) INFORMATION FOR SEQ ID NO:138
15 -	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20 .	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:138:
25	Ser Leu Pro Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Lys Leu 1 5 10 15
•	(139) INFORMATION FOR SEQ ID NO:139
30	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
•	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:
	Ser Leu Pro Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Asn Lys Leu 1 5 10 15
45	(140) INFORMATION FOR SEQ ID NO:140
	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

Ser Leu Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Ser Glu Lys Leu 1 5 10 15

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- (141) INFORMATION FOR SEQ ID NO:141
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

Ser Leu Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Ser Asp Lys Leu
1 5 10 15

(142) INFORMATION FOR SEQ ID NO:142

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:

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- Ser Leu Pro Pro Arg Pro Gly Arg Val Arg Ser Ser Ser Glu Lys Leu
 1 5 10 15
- 40 (143) INFORMATION FOR SEQ ID NO:143
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

Ser Leu_Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Glu Gln Leu
1 5 10 15

- (144) INFORMATION FOR SEQ ID NO:144
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:144: Ser Leu Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Ser Glu Thr Leu 10 (145) INFORMATION FOR SEQ ID NO:145 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:145: 25 Ser Leu Pro Pro Lys Pro Gly Lys Ile Arg Ser Ser Thr Gly Lys Leu (146) INFORMATION FOR SEQ ID NO:146 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 35 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:146: Ser Leu Pro Pro Lys Pro Gly Arg Ile Arg Ser Ser Thr Gly Lys Leu 45 (147) INFORMATION FOR SEQ ID NO:147 (i) SEQUENCE CHARACTERISTICS: 50 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:147:

Ser Leu Pro Pro Lys Pro Gly Lys Ile Arg Ser Ser Thr Gly Gln Leu 1 5 10 15

(148) INFORMATION FOR SEQ ID NO:148

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:148:
- Ser Leu Pro Pro Glu Pro Gly Lys Ile Arg Ser Ser Thr Gly Arg Leu
 1 5 10 15
 - (149) INFORMATION FOR SEQ ID NO:149
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:149:
 - Ser Leu Ala Pro Ser Pro Gly Lys Ile Arg Ser Thr Ala Glu Lys Leu .1 10 15
- 40 (150) INFORMATION FOR SEQ ID NO:150
 - (i) SEQUENCE CHARACTERISTICS: .
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:150:
 - Ser Leu Pro Pro Arg Pro Gly Lys Ile Arg Ser Ser Thr Gly Asn Val
 - (151) INFORMATION FOR SEQ ID NO:151
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:151: Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Lys Leu 10 (152) INFORMATION FOR SEQ ID NO:152 (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:152: 25 Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Asp Lys Leu (153) INFORMATION FOR SEQ ID NO:153 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 35 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:153: 40 Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Asn Leu 45 (154) INFORMATION FOR SEQ ID NO:154 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 50 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:154: 55

Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Ala Val Glu Lys Leu 1 5 10 15

5 (155) INFORMATION FOR SEQ ID NO:155 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 15 amino acids 10 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:155: Ser Leu Pro Pro Arg Pro Gly Lys Arg Ser Ser Ala Glu Lys Leu 1 20 (156) INFORMATION FOR SEQ ID NO:156 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 30 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:156: 35 Ser Leu Ala Pro Ser Pro Gly Lys Val Arg Ser Thr Val Glu Arg Leu (157) INFORMATION FOR SEQ ID NO:157 40 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 45 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:157: 50 Ser Leu Ala Pro Ser Pro Asp Lys Ile Arg Ser Thr Pro Asp Lys Leu

(158) INFORMATION FOR SEQ ID NO:158

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(i) SEQUENCE CHARACTERISTICS:

	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:158:
10	Ser Leu_Ala Leu Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Lys Leu 1 10 15
	(159) INFORMATION FOR SEQ ID NO:159
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:159:
25	Ser Leu Pro Leu Ser Ala Gly Lys Val Arg Ser Thr Ala Glu Lys Leu 1 5 10 15
30	(160) INFORMATION FOR SEQ ID NO:160 (i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:160:
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:160: Ser Leu Ala Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Tyr Leu 1 5 10 15
45	Ser Leu Ala Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Tyr Leu
45	Ser Leu Ala Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Tyr Leu 1 5 10 15
45 50	Ser Leu Ala Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Tyr Leu 1 5 10 15 (161) INFORMATION FOR SEQ ID NO:161
	Ser Leu Ala Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Tyr Leu 1 5 10 15 (161) INFORMATION FOR SEQ ID NO:161 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid

Ser Leu Pro Leu Thr Pro Gly Leu Ile Arg Ser Thr Ala Glu Lys Leu

(162) INFORMATION FOR SEQ ID NO:162 5 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 10 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:162: Ser Leu Pro Leu Thr Pro Arg Val Ile Arg Ser Thr Ala Glu Lys Leu 20 (163) INFORMATION FOR SEQ ID NO:163 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:163: Phe Leu His Pro Thr Pro Gly Thr Asp Ser Ser Ser Thr Glu Lys Leu 35 1 15 (164) INFORMATION FOR SEQ ID NO:164 (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY, linear 45 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:164: 50 Phe Leu Leu Pro Thr Pro Gly Thr Asp Ser Ser Ser Thr Glu Arg Leu 10 (165) INFORMATION FOR SEQ ID NO:165

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

	(B) TYPE: amino acid (C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:165:
10	Phe Leu His Pro Thr Arg Val Thr Asp Ser Ser Ser Thr Glu Lys Leu 1 5 10 15
15	(166) INFORMATION FOR SEQ ID NO:166 (i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:166:
	Leu Leu Pro Pro Thr Pro Gly Thr Asn Ser Ser Ser Asn Asp Lys Leu 1 5 10 15
30	(167) INFORMATION FOR SEQ ID NO:167
•	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:167:
45	Val Leu Pro Leu Ser Pro His Arg Ile Arg Ser Glu Ser Glu Asn Leu 1 5 10 15
	(168) INFORMATION FOR SEQ ID NO:168
50	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(vi) SECUENCE DESCRIPTION: SEC ID NO:168:

Ser Leu Ala Pro Ser Pro Ala Lys Phe Arg Ser Thr Ala Glu Arg Asp (169) INFORMATION FOR SEQ ID NO:169 5 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 10 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:169: 15 Val Thr Ala Pro Arg Pro Gly Arg Ile Arg Ser Asp Pro Glu Lys Lys 10 20 (170) INFORMATION FOR SEQ ID NO:170 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY. linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:170: Val Thr Ala Pro Arg Pro Gly Arg Val Arg Ser Asp Pro Glu Lys Lys 35 (171) INFORMATION FOR SEQ ID NO:171 40 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 45 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:171: 50 Val Thr Gly Pro Arg Pro Gly Arg Ile Arg Ser Asp Pro Glu Lys Lys 55 (172) INFORMATION FOR SEQ ID NO:172

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ.ID NO:172: Val Thr Gly Pro Arg Pro Gly Arg Ile Arg Ser Asp Pro Asp Lys Lys 10 (173) INFORMATION FOR SEQ ID NO:173 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:173: 25 Val Thr Gly Pro Arg Pro Gly Arg Val Arg Ser Asp Pro Glu Lys Lys (174) INFORMATION FOR SEQ ID NO: 174 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 35 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:174: Val Thr Gly Pro Arg Pro Gly Arg Ile Arg Ser Asp Pro Xaa Lys Lys 45 (175) INFORMATION FOR SEQ ID NO:175 (i) SEQUENCE CHARACTERISTICS: 50 . (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:175: 55

	Val Thr Ala Pro Arg Pro Gly Arg Ile Arg Ser Glu Ser Glu Arg Lys 1 5 10 15
5	(176) INFORMATION FOR SEQ ID NO:176
	(i) SEQUENCE CHARACTERISTICS:
10	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:176:
20	Val Thr Gly Pro Ser Arg Gly Arg Ile Arg Ser Asp Pro Glu Lys Lys 1 5 10 15
	(177) INFORMATION FOR SEQ ID NO:177
	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
,	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:177:
35	Val Thr Val Pro Arg Pro Ser Arg Ile Arg Ser Glu Ser Glu Arg Lys 1 5 10 15
	(178) INFORMATION FOR SEQ ID NO:178
40	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
_, 45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:178:
50	Val Thr Ala Pro Gly Pro Gly Arg Ile Arg Ser Glu Ser Glu Arg Lys 1 5 10 15
55	(179) INFORMATION FOR SEQ ID NO:179
-	(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

	(B) TYPE: amino acid (C) TOPOLOGY: linear	
r.	(ii) MOLECULE TYPE: peptide	
5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:179:	
10	Gln Thr Ser Val Arg Pro Gly Arg Val	Arg Ser Asp Pro Glu Arg Lys 10 15
	(180) INFORMATION FOR SEQ ID NO:180	
15	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear	
20	(ii) MOLECULE TYPE: peptide	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:180:	
25	Gln Thr Ser Val Arg Pro Gly Lys Val	Arg Ser Asp Pro Glu Arg Lys 10 15
	(181) INFORMATION FOR SEQ ID NO:181	9
30	(i) SEQUENCE CHARACTERISTICS:	
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
50	(ii) MOLECULE TYPE: peptide	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:181:	
40	Gln Thr Ser Val Arg Pro Gly Lys Va.	l Arg Ser Asp Pro Glu Lys Lys 10 15
45	(182) INFORMATION FOR SEQ ID NO:182	
-	(i) SEQUENCE CHARACTERISTICS:	
50	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	•
55	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:182:	••
	Gln Thr Ser Val Arg Pro Gly Lys Val	Arg Ser Glu Pro Glu Lys Lys

(183) INFORMATION FOR SEQ ID NO:183

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 5 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:183: Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Glu Pro Asp Lys Lys 15 (184) INFORMATION FOR SEQ ID NO:184 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:184: Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ala Glu Pro Glu Lys Lys 30 (185) INFORMATION FOR SEQ ID NO:185 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:185: Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asx Pro Glx Lys Lys 1 10 15 (186) INFORMATION FOR SEQ ID NO:186 50 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH; 16 amino acids (B) TYPE: amino acid 55 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:186:

Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Asx Lys Lys 5 10 (187) INFORMATION FOR SEQ ID NO:187 (i) SEQUENCE CHARACTERISTICS: 10 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 15 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:187: 20 Gln Thr Ser Val Arg Pro Gly Gln Val Arg Ser Asp Pro Glu Arg Lys (188) INFORMATION FOR SEQ ID NO:188 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 30 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:188: Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser His Pro Glu Lys Lys 40 (189) INFORMATION FOR SEQ ID NO:189 (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 50 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:189: 55 Gln Thr Ser Val Arg Pro Gly Asn Val Arg Ser Asp Pro Asp Lys Lys

(190) INFORMATION FOR SEQ ID NO:190

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 5 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:190: Gin Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Glu Lys Thr 15 (191) INFORMATION FOR SEQ ID NO:191 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:191: Gln Thr Ser Val Arg Pro Gly Thr Val Arg Ser Glu Pro Glu Lys Lys 30 (192) INFORMATION FOR SEQ ID NO:192 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide .(xi) SEQUENCE DESCRIPTION: SEQ ID NO:192: 45 Gln Thr Ser Val Arg Pro Glu Lys Val Arg Ser Glu Pro Asp Lys Lys 1 (193) INFORMATION FOR SEQ ID NO:193 50 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid 55 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:193:

Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Glu Ser Asp Lys Lys

1 10 15

(194) INFORMATION FOR SEQ ID NO:194

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:194:

Gln Thr Ser Val Arg Pro^Gly Glu Val Arg Ser Glu Pro Asp Lys Lys

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(195) INFORMATION FOR SEQ ID NO:195

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:195:

Gln Thr Ser Val Arg Pro Gly Asx Val Arg Ser Asx Pro Glx Arg Lys

1 10 15

- 40 (196) INFORMATION FOR SEQ ID NO:196
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:196:

Gin Thr Ser Val Ser Pro Gly Lys Val Arg Ser Asp Pro Glu Lys Lys
1 10 15

- (197) INFORMATION FOR SEQ ID NO:197
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:197: Gln Thr Ser Val Arg Pro Gly Lys Val Asn Ser Asp Pro Glu Lys Lys 10 (198) INFORMATION FOR SEQ ID NO:198 15 (i) SEQUENCE CHARACTERISTICS: . (A) LENGTH: 16 amino acids (B) TYPE: amino acid 20 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:198: 25 Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Asp Thr Lys (199) INFORMATION FOR SEQ ID NO:199 30 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids 35 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:199: Val Arg Pro Lys Lys Val Arg Ser Asp Pro Glx Lys Lys 45 (200) INFORMATION FOR SEQ ID NO:200 (i) SEQUENCE CHARACTERISTICS: 50 (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:200:

Gln Thr Ser Val Arg Pro Lys Lys Val Arg Phe Asp Pro Glu Lys Lys 1 5 10 15

(201) INFORMATION FOR SEQ ID NO:201

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:201:
- Gln Thr Ser Val Arg Ser Gly Lys Val Arg Ser Glu Pro Glu Thr Lys

 1 5 10 15

(202) INFORMATION FOR SEQ ID NO:202

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:202:
- Val Thr Asn Leu Arg Pro Gly Lys Val Arg Ser Asp Ala Glu Lys Lys
- (203) INFORMATION FOR SEQ ID NO:203
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 16 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:203:

Val Thr Asp Leu Arg Pro Gly Lys Val Arg Ser Asp Ala Glu Lys Lys
1 10 15

- 55 (204) INFORMATION FOR SEQ ID NO:204
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear

5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:204:
10	Gln Thr Ser Val Ser Pro Gly Asn Ile Arg Ser Glu Ser Asp Lys Lys 1 5 10 15
15	(205) INFORMATION FOR SEQ ID NO:205 (i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:205:
-	Lys Thr Ser Val Thr Pro Gly Lys Phe Arg Ser Glu Pro Glu Lys Lys 1 5 10 15
30	(206) INFORMATION FOR SEQ ID NO:206
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:206:
45	Val Thr Leu Leu Pro Pro Gly Arg Val Arg Ser Asp Ala Glu Lys Lys 1 5 10 15
	(207) INFORMATION FOR SEQ ID NO:207
50	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:207:

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(i) SEQUENCE CHARACTERISTICS:

Val Thr Leu Leu Pro Pro Gly Glu Val Arg Ser Asp Ala Glu Lys Lys (208) INFORMATION FOR SEQ ID NO:208 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:208: Val Thr Leu Pro Pro Pro Gly Glx Val Arg Ser Asp Ala Glu Arg Lys (209) INFORMATION FOR SEQ ID NO:209 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:209: Val Thr Leu Pro Pro Pro Gly Glx Val Arg Ser Asx Ala Glx Asn Lys (210) INFORMATION FOR SEQ ID NO:210 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:210: Val Thr Leu Pro Pro Pro Gln Gln Val Arg Ser Asp Ala Glu Lys Lys (211) INFORMATION FOR SEQ ID NO:211

(A) LENGTH: 16 amino acids

	(B) TYPE: amino acid (C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:211:
10	Val Thr Leu Pro Pro Pro Gly Gln Val Thr Ser Asp Ala Glu Lys Lys 1 5 10 15
	(212) INFORMATION FOR SEQ ID NO:212
15	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE-DESCRIPTION: SEQ ID NO:212:
25	
	Val Thr Leu Pro Pro Ala Gly Gln Val Arg Ser Asp Ala Glu Lys Arg 1 5 10 15
30	(213) INFORMATION FOR SEQ ID NO:213
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 16 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
•	(ii) MOLECULE TYPE: peptide
40.	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:213:
45	Ala Leu Ser Pro Ser Ser Gly Gln Ser Ser Ser Ala Ser Glu Arg Leu 1 5 10 15
	(214) INFORMATION FOR SEQ ID NO:214
50	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
55	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:214:

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1 5 10 15 15	a.
Ser Arg Gly Asp Ser Gln Arg Pro Glu Ser 20 25	
(215) INFORMATION FOR SEQ ID NO:215	
(i) SEQUENCE CHARACTERISTICS:	
(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
(ii) MOLECULE TYPE: peptide	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:215:	
Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys v 1 5 10 15	
Ser Arg Gly Asp Ser Gln Arg Pro Glu Ser 20 25	
(216) INFORMATION FOR SEQ ID NO:216	
(i) SEQUENCE CHARACTERISTICS:	
(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
(ii) MOLECULE TYPE: peptide	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:216:	
Glu Lys Val Gly Gly Leu Gln Pro Gly Thr Gly Ala Pro Gly Lys Al 1 5 10 15	La
Ser Arg Gly Asp Ser Gln Arg Pro Glu Ser 20 25	•
(217) INFORMATION FOR SEQ ID NO:217	
(i) SEQUENCE CHARACTERISTICS:	
(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
(ii) MOLECULE TYPE: peptide	

	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:217:
5	Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala 1 5 10 15
	Ser Lys Gly Asn Ser Gln Arg Ala Glu Ser 20 25
10	(218) INFORMATION FOR SEQ ID NO:218
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:218:
25	Glu Lys Met Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Al 1 5 10 15
30 ·	Ser Lys Gly Asn Ser Gln Arg Ala Glu Ser 20 25
30	(219) INFORMATION FOR SEQ ID NO:219
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:219:
45	Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala 1 5 10 15
•	Ser Lys Gly Thr Ser Gln Arg Ala Glu Ser 20 25
50	(220) INFORMATION FOR SEQ ID NO:220

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear

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(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:220: 5 Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr 10 (221) INFORMATION FOR SEQ ID NO:221 (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:221: 25 Glu Lys Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Gly Lys Ala 15 30 Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr 20 (222) INFORMATION FOR SEQ ID NO:222 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:222: 45 Glu Asn Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala 50 Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr 20 (223) INFORMATION FOR SEQ ID NO:223 55

(i) SEQUENCE CHARACTERISTICS:

-(A) LENGTH: 26 amino acids

	(B) TYPE: amino acid (C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:223:
10	Glu Lys Val Gly Gly Leu Gln Ser Gly Arg Gly Thr Pro Gly Lys Ala 1 15
	Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr. 20 25
15	(224) INFORMATION FOR SEQ ID NO:224
	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:224:
30	Glu Lys Val Gly Gly Leu Gln Ser Gly Arg Gly Thr Pro Gly Lys Ala 1 5 10 15
	Ser Lys Gly Thr Ser Gln Arg Ala Glu Ser 20 25
35	
	(225) INFORMATION FOR SEQ ID NO:225
	(225) INFORMATION FOR SEQ ID NO:225 (i) SEQUENCE CHARACTERISTICS:
40	
40 45	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid
	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide
45	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:225: Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:226: Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ser 10 Ala Lys Gly Asx Ser Glx Arg Ala Gln Ser 15 (227) INFORMATION FOR SEQ ID NO:227 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:227: Glu Lys Val Gly Gly Leu Gln Pro Gly Ser Gly Thr Pro Gly Lys Ala 30 Ser Lys Gly Asn Ser Gln Arg Ala Glu Ser 20 35 (228) INFORMATION FOR SEQ ID NO:228 (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:228: Glu Lys Val Gly Gly Leu Gln Pro Gly Ser Gly Thr Pro Gly Lys Ala Ser Lys Gly Ser Ser Gln Arg Ala Glu Ser 25 20 55 (229) INFORMATION FOR SEQ ID NO:229

	(i) SEQUENCE CHARACTERISTICS:
5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:229:
	Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Arg Lys Al 1 5 10 15
15	Ser Lya Gly Asn Ser Gln Arg Ala Glu Ser 20 25
20	(230) INFORMATION FOR SEQ ID NO:230
	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:230:
35	Glu Lys Met Gly Asn Leu Gln Pro Gly Ser Gly Thr Pro Gly Lys Ala 1 5 10 15
	Ser Lys Gly Asn Ser Gln Arg Pro Asp Ser 20 25
40	(231) INFORMATION FOR SEQ ID NO:231
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:231:
55	Glu Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
	Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr 20 25

(232) INFORMATION FOR SEQ ID NO:232

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid

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- (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:232:

Glu Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Ala Pro Glu Lys Asp 1 5 10 15

Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr 20 25

(233) INFORMATION FOR SEQ ID NO:233

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - . (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:233:

Glu Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Arg Asp.

1 10 15

Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr 20 · 25

(234) INFORMATION FOR SEQ ID NO:234

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:234:

	Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
5	Ser Lys Gly Asn Ala Lys Arg Ser Glu Thr 20 25
10	(235) INFORMATION FOR SEQ ID NO:235 (i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:235:
	Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 10 15
	Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
20	(236) INFORMATION FOR SEQ ID NO:236
30	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:236:
	Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Asp Lys Asp 1 10 15
45	Asn Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
50	(237) INFORMATION FOR SEQ ID NO:237
	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:237:
5	Glu Lys Val Gly Gly Leu Thr Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10
	Ser Lys Gly Asn Gly Arg Arg Ser Glu Thr 20 25
10	(238) INFORMATION FOR SEQ ID NO:238
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:238:
25	Glu Met Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
: .	Ser Lys Gly Asn Asp Arg Arg Ser Glu Thr 20 25
30	(239) INFORMATION FOR SEQ ID NO:239
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:239:
45	Glu Met Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
50	Ser Lys Gly Asn Asp Lys Arg Ser Glu Thr 20 25
50	(240) INFORMATION FOR SEQ ID NO:240

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(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

	(ii) MOLECULE TYPE: peptide	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:240:	
5	Glu Met Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15	
10	Ser Lys Gly Asn Ala Lys Arg Ser Glu Thr 20 25	
	(241) INFORMATION FOR SEQ ID NO:241	
15	(i) SEQUENCE CHARACTERISTICS:	
20	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
20	(ii) MOLECULE TYPE: peptide	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:241:	
25		
	Glu Gln Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15	
30	Ser Lya Gly Asn Ala Lys Lys Ser Glu Thr 20 25	
35	(242) INFORMATION FOR SEQ ID NO:242	
	(i) SEQUENCE CHARACTERISTICS:	
40	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:242:	
	Glu Gln Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys As	E
50	Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr	
66	(243) INFORMATION FOR SEQ ID NO:243	
55	(i) SEQUENCE CHARACTERISTICS:	

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear

5	(ii) MOLECULE TYPE: peptide
J	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:243:
10	Glu Gln Val Gly Gly Leu Lys Pro Gly Lys Gly Ala Pro Glu Lys Asp 1 5 10 15
	Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
15	(244) INFORMATION FOR SEQ ID NO:244
	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:244:
30	Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
35	Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
	(245) INFORMATION FOR SEQ ID NO:245
	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:245:
50	Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
	Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
55	
	(246) INFORMATION FOR SEQ ID NO:246
	(246) INFORMATION FOR SEQ ID NO:246 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

5 ·	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:246:
10	Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Glu Lys Asp 1 5 10 15
15	Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
	(247) INFORMATION FOR SEQ ID NO:247
20	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:247:
30	Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Ser Pro Glu Lys Asp 1 5 10 15
35	Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
	(248) INFORMATION FOR SEQ ID NO:248
40	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:248:
50	Asp Lys Met Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
55	Ser Lys Gly Asn Ala Lys Gln Ser Glu Thr 20 25
	(249) INFORMATION FOR SEQ ID NO:249

(i) SEQUENCE CHARACTERISTICS:

5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:249:
	Glu Gln Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Asp Lys Asp 1 5 10 15
15	Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25
20	(250) INFORMATION FOR SEQ ID NO:250
20	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:250:
	Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
35	Ser Lys Gly Asn Ala Glu Lys Ser Glu Thr 20 25
	(251) INFORMATION FOR SEQ ID NO:251
40	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:251:
	Glu Gln Val Gly Asp Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
55	Thr Lys Gly Asn Ala Arg Arg Ser Glu Thr 20 25

(252) INFORMATION FOR SEQ ID NO:252

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(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:252: Glu Asn Val Gly Asp Leu Lys Pro Gly Lys Gly Ala Pro Glu Lys Asp 15 Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr 20 (253) INFORMATION FOR SEQ ID NO:253 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:253: Glu Gln Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Ser Asp Lys Asp 1 10 15 35 Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 40 (254) INFORMATION FOR SEQ ID NO:254 (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:254:

	1 5 10	15
5	Ser Lys Gly Asn Ala Lys Lys Ser Gly Thr 20 25	
10	(255) INFORMATION FOR SEQ ID NO:255	
	(i) SEQUENCE CHARACTERISTICS:	
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:255:	
	Asp Gln Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu 1 5 10	Lys Asp
25	Thr Lys Gly Asn Pro Lys Arg Ser Glu Thr 20 25	
30	(256) INFORMATION FOR SEQ ID NO:256	
30	(i) SEQUENCE CHARACTERISTICS:	
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:256:	
	Asp Gln Val Gly Gly Leu Gln Pro Gly Gln Gly Thr Pro Glu 1	Lys Asn 15
45	Thr Lys Gly Asn Pro Lys Arg Ser Asp Thr 20 25	
	(257) INFORMATION FOR SEQ ID NO:257	
50	(i) SEQUENCE CHARACTERISTICS:	
55	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	

Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Ser Glu Lys Asp
1 5 10 15

Ile Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:257:

(258) INFORMATION FOR SEQ ID NO:258

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:258:
- Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Arg Thr Pro Glu Lys Asp
 1 5 10 15
 - Asn Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25

(259) INFORMATION FOR SEQ ID NO:259

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:259:
- Asp Lys Val Gly Gly Leu Lys Leu Gly Lys Gly Thr Pro Glu Lys Asp

Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr 20 25

- (260) INFORMATION FOR SEQ ID NO:260
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:260:
i	Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys As 1 5 10 15
o	Ser Lys Gly Asn Ala Asn Thr Ser Glu Thr 20 25
	(261) INFORMATION FOR SEQ ID NO:261
5	(i) SEQUENCE CHARACTERISTICS:
2	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
U	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:261:
5	Glu His Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asr 1 5 10 15
0	Ser Lys Gly Asn Ala Gly Arg Ser Glu Thr 20 25
	(262) INFORMATION FOR SEQ ID NO:262
5	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
0	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:262:
5	Glu Gln Val Gly Gly Leu Gln Pro Gly Asn Gly Thr Pro Glu Lys Asp 1 5 10 15
0	Thr Thr Gly Asn Ala Lys Arg Ser Glu Thr 20 25
	(263) INFORMATION FOR SEQ ID NO:263
5	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:263: Glu Lys Glu Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Glu 10 Ser Lys Gly Asp Ser Lys Arg Ala Glu Thr (264) INFORMATION FOR SEQ ID NO:264 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 20 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:264: Glu Lys Glu Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Glu 30 Ser Lys Gly Asp Ser Lys Arg Pro Glu Thr 35 (265) INFORMATION FOR SEQ ID NO:265 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 40 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:265: Glu Lys Glu Gly Gly Leu Gln Pro Gly Lys Gly Ser Pro Glu Lys Glu 50 Ser Lys Gly Asp Ser Lys Arg Ala Glu Thr (266) INFORMATION FOR SEQ ID NO:266 55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:266: Glu Lys Asp Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp 10 Ser Lys Gly Asp Ser Lys Arg Val Glu Met 25 15 (267) INFORMATION FOR SEQ ID NO:267 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:267: 30 Glu Gln Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Glu Lys Asp Thr Thr Gly Asp Ala Gln Arg Ser Glu Thr 35 (268) INFORMATION FOR SEQ ID NO:268 (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:268: 50 Glu Gln Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Glu Lys Asp Thr Thr Gly Asn Ala Lys Gly Ser Glu Thr 20 25 55 (269) INFORMATION FOR SEQ ID NO:269

(i) SEQUENCE CHARACTERISTICS:

	·
5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:269:
10	Glu Lys Val Gly Gly Ser Lys Pro Gly Lys Gly Thr Pro Glu Lys As
15	Ser Lys Gly Asn Ala Lys Thr Ser Glu Thr 20 25
20	(270) INFORMATION FOR SEQ ID NO:270
20	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:270:
	Ser Asp Gln Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp 1 5 10 15
35	Thr Lys Gly Asn Ala Arg Arg Ser Glu Ser 20 25
40	(271) INFORMATION FOR SEQ ID NO:271
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:271:
	Glu Lys Ile Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Pro 1 5 10 15
55	Ser Lys Asp Asn Ala Lys Arg Ser Glu Thr

(272) INFORMATION FOR SEQ ID NO:272

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(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 5 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:272: Glu Lys Leu Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Pro 1 15 Ser Lys Asp Asn Ala Lys Arg Ser Glu Thr 20 (273) INFORMATION FOR SEQ ID NO:273 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:273: Glu Lys Leu Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Pro 35 Phe Lys Asp Asn Ala Lys Arg Ser Glu Thr 25 20 40 (274) INFORMATION FOR SEQ ID NO:274 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 45 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:274:

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(ii) MOLECULE TYPE: peptide

Glu Lys Leu Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Leu 1 10 15
Met Lys Glu Asn Ala Lys Arg Ser Glu Thr 20 25
(275) INFORMATION FOR SEQ ID NO:275
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:275:
Glu Asn Leu Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Let 1 5 10 15
Lys Xaa Glu Asn Ala Lys Arg Pro Glu Thr 20 25
(276) INFORMATION FOR SEQ ID NO:276
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
(ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:276:
Glu Lys Leu Gly Gly Leu Gln Pro Gly Asn Gly Asp Leu Gly Lys Pro 1 5 10
Ser Lys Asp Asn Ala Lys Arg Ser Glu Thr 20 25
(277) INFORMATION FOR SEQ ID NO:277
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:277:
5	Glu Lys Leu Gly Pro Leu Gln Leu Gly Lys Gly Asp Pro Gly Lys Pro 1 5 10 15
	Ser Lya Asp Asp Ala Lys Arg Ser Glu Thr 20 25
10	(278) INFORMATION FOR SEQ ID NO:278
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:278:
25	Glu Gln Leu Gly Gly Leu Gln Pro Gly Gly Gly Thr Pro Gly Lys Pr 1 5 10 15
	Ser Lys Asp Asn Asp Lys Arg Ser Glu Thr 20 25
30	(279) INFORMATION FOR SEQ ID NO:279
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:279:
45	Glu Gln Leu Gly Gly Leu Gln Pro Gly Gly Gly Thr Pro Gly Lys Ala 1 5 10 15
	Ser Lys Asp Asn Asp Lys Arg Ser Glu Thr 20 25
50	(280) INFORMATION FOR SEQ ID NO:280

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:280: 5 Glu Gln Val Gly Gly Leu Lys Ala Arg Lys Gly Thr Pro Glu Lys Asp Thr Thr Gly Asn Ala Lys Arg Ser Glu Thr 10 (281) INFORMATION FOR SEQ ID NO:281 (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:281: 25 Glu Met Val Gly Val Leu Glu Pro Gly Lys Gly Thr Pro Glu Lys Arg 10 Gln Glu Gly Asn Ala Lys Arg Ser Glu Thr 30 20 (282) INFORMATION FOR SEQ ID NO:282 (i) SEQUENCE CHARACTERISTICS: 35 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:282: 45 Glu Gln Val Gly Gly Leu Gln Pro Lys Lys Gly Ser Pro Gly Lys Asp Ser Lys Asp Asp Ser Gln Lys Thr Glu Thr 50 20 (283) INFORMATION FOR SEQ ID NO:283 (i) SEQUENCE CHARACTERISTICS: 55

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:283: 5 Glu Gln Val Gly Gly Leu Gln Pro Lys Lys Gly Ser Pro Gly Lys Asp 10 Ser Lys Asp Asp Ser Gln Lys Thr Glu Arg 15 (284) INFORMATION FOR SEQ ID NO:284 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid 20 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:284: 25 Gln Gln Val Pro Glu Leu Lys Pro Gly Arg Gly Thr Pro Gly Lys Glu 30 Asp Lys Gly Thr Ser Ala Arg Asn Asp Thr 20 (285) INFORMATION FOR SEQ ID NO:285 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid 40 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:285: 45 Gln Gln Val Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Lys Asp 1 50 Asp Lys Gly Thr Ser Ala Lys Asn Glu Thr 20

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(286) INFORMATION FOR SEQ ID NO:286

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

	(B) TYPE: amino acid (C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:286:
10	Gln Gln Val Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Lys Asp 1 5 10 15
15	Asp Lya Gly Thr Ser Ala Lys Asn Glu Met 20 25
	(287) INFORMATION FOR SEQ ID NO:287
20	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:287:
30	Gln Gln Lys Pro Glu Leu Lys Pro Gly Lys Gly Ser Pro Gly Gln Glu 1 5 10 15
35	Lys Lys Gly Thr Ser Ser Thr Ser Glu Thr 20 25
	(288) INFORMATION FOR SEQ ID NO:288
40	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:288:
50	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu 1 5 10 15
55	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25
	(289) INFORMATION FOR SEQ ID NO:289

•	(i) SEQUENCE CHARACTERISTICS:
5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:289:
	Glu Gln Gln Pro Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Glu 1 5 10 15
15	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25
	(290) INFORMATION FOR SEQ ID NO:290
20	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:290:
	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu 1 5 10 15
35	Lys Lys Gly Lys Ser Ser Ala Ser Glu Ser 20 25
40	(291) INFORMATION FOR SEQ ID NO:291
	(i) SEQUENCE CHARACTERISTICS:
45	-(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:291:
55	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Lys Gln 1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser

(292) INFORMATION FOR SEQ ID NO:292

	(i) Sequence Characteristics.
5	(A) LENGTH: 26 amino acids
	(B) TYPE: amino acid
10	(C) TOPOLOGY: linear
10	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:292:
15	
	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln 1 5 10 15
20	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25
	(293) INFORMATION FOR SEQ ID NO:293
25	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
30	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:293:
35	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Ser His Gly Lys Gln 1 5 10 15
40	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25
	(294) INFORMATION FOR SEQ ID NO:294
45	(i) SEQUENCE CHARACTERISTICS:
50	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
50	(ii) MOLECULE TYPE: peptide
	/ (xi) SEQUENCE DESCRIPTION: SEQ ID NO:294:
55	

	1 5 10 15
5	Lys Lys Gly Lys Ser Ser Ala Ser Glu Ser 20 25
10	(295) INFORMATION FOR SEQ ID NO:295
15	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:295:
	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln 1 10 15
25	Lys Lys Gly Lys Ser Ser Thr Phe Glu Ser 20 25
, 30	(296) INFORMATION FOR SEQ ID NO:296
-	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
1 0	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:296:
	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln 1 5 10 15
45	Lys Gln Gly Lys Ser Ser Thr Phe Glu Ser 20 25
50	(297) INFORMATION FOR SEQ ID NO:297
	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:297:
5	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Glu 1 5 10 15
40	Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser 20 25
10	(298) INFORMATION FOR SEQ ID NO:298
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:298:
25 .	Glu Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Ser His Gly Lys Gln 1 5 10 15
30	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25
	(299) INFORMATION FOR SEQ ID NO:299
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
40	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:299:
45	Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln 1 5 10 15
50	Lys Lys Ser Asn Ser Ser Thr Ser Glu Ser 20 25
	(300) INFORMATION FOR SEQ ID NO:300
	(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ.ID NO:300: 5 Gin Gin Gin Ala Glu Leu Arg Pro Gly Lys Gly Ala Pro Gly Glu Glu Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 10 (301) INFORMATION FOR SEQ ID NO:301 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:301: 25 Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Ala Pro Gly Gln Glu Lys Lys Gly Lys Ser Ser Thr Ser Asp 30 (302) INFORMATION FOR SEQ ID NO:302 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:302: 45 Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Val Pro Gly Gln Glu 1 Lys Lys Gly Lys Ser Ser Thr Ser Asp Ser 50 20 (303) INFORMATION FOR SEQ ID NO:303 55 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear

	(ii) Moccoocc 111 L. pepide
5	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:303:
10	Gln Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Ala Pro Gly Lys Gly 1 10 15
	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25
15	(304) INFORMATION FOR SEQ ID NO:304
	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:304:
30	Gln Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Ala Pro Gly Lys Gly 1 5 10 15
	Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser 20 25
35	(305) INFORMATION FOR SEQ ID NO:305
	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:305:
50	Glu Gln Gln Pro Glu Ala Lys Pro Gly Lys Gly Thr His Gly Lys Gln 1 5 10 15
	Lys Lys Gly Lys Ser Ser Thr Ser Asp Ser 20 25
55	(306) INFORMATION FOR SEQ ID NO:306
	(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:306: Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Glu 10 Lys Lys Asp Lys Ser Ser Thr Ser Asp Ser 15 (307) INFORMATION FOR SEQ ID NO:307 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:307: Gin Gin Gin Ala Glu Leu Arg Pro Gly Lys Gly Ala Pro Gly Gin Gly 30 Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 35 (308) INFORMATION FOR SEQ ID NO:308 (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:308: Gln Gln Gln Ala Glu Leu Lys Pro Gly Arg Gly Thr Pro Gly Gln Glu 50 .1 10 15 Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 55 (309) INFORMATION FOR SEQ ID NO:309

(i) SEQUENCE CHARACTERISTICS:

5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:309:
	Glu Gln Gln Ala Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu 1 5 10 15
15	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25
20	(310) INFORMATION FOR SEQ ID NO:310
20	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:310:
	Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Glu 1 5 10 15
35	Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser 20 25
	(311) INFORMATION FOR SEQ ID NO:311
40 -	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:311:
	Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly His Gl 1 5 10 15
55	Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser

(312) INFORMATION FOR SEQ ID NO:312 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 5 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:312: Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly His Glu 15 Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser 20 (313) INFORMATION FOR SEQ ID NO:313 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 25 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:313: Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly His Glu 35 Asn Lys Gly Thr Ser Ser Thr Ser Glu Ser 20 25 4Ò (314) INFORMATION FOR SEQ ID NO:314 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 45 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:314:

•	1 5 10 15 15 10 10 15 15 15 16 16 16 16 16 16 16 16 16 16 16 16 16
5	Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser 20 25
10	(315) INFORMATION FOR SEQ ID NO:315
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:315:
25	Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly His Glu 1 5 10 15
	Asn Lys Gly Thr Ser Ser Thr Ser Glu Ser 20 25
30	(316) INFORMATION FOR SEQ ID NO:316
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:316:
45	Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Gln 1 5 10 15
	Lys Lys Gly Lys Ser Ser Ala Ser Glu Ser 20 25
50	(317) INFORMATION FOR SEQ ID NO:317
	(i) SEQUENCE CHARACTERISTICS:
55	(A) L'ENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: popiido

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:317:

His Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25

(318) INFORMATION FOR SEQ ID NO:318

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:318:

Glu Gln Gln Val Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser

- (319) INFORMATION FOR SEQ ID NO:319
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:319:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 10 15

Lys Gln Gly Thr Ser Ser Thr Ser Glu Ser
20 25

- (320) INFORMATION FOR SEQ ID NO:320
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:320: 5 Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly His Asp 10 Asn Lys Gly Thr Ser Ser Thr Ser Glu Ser 20 (321) INFORMATION FOR SEQ ID NO:321 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:321: Gin Gin Gin Ala Glu Val Arg Pro Gly Lys Gly Thr Pro Gly 15 30 Lys Lys Gly Arg Ser Ser Thr Ser Glu Ser (322) INFORMATION FOR SEQ ID NO:322 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:322: 45 Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Gln. Lys Ser Ser Thr Ser Glu Ser (323) INFORMATION FOR SEQ ID NO:323 55 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:323: Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln 10 Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser 20 15 (324) INFORMATION FOR SEQ ID NO:324 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:324: 30 Gin Gin Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gin Gin. 15 Lys Lys Asp Lys Ser Ser Thr Ser Asp Ser 35 (325) INFORMATION FOR SEQ ID NO:325 (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 26 amino acids (B) TYPE: amino acid. (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:325: 50 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Ser Pro Gly Gln Gln 1 Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser 25 .20 55

(326) INFORMATION FOR SEQ ID NO:326

	(i) SEQUENCE CHARACTERISTICS:	the state of the s
5 .	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:326:	
	Gln His Gln Ala Glu Leu Lys Pro Gly I	ys Gly Thr Pro Gly Gln Gl 10 15
15	Lys Lys Asn Lys Ser Ser Thr Ser Glu 20 25	Ser
20	(327) INFORMATION FOR SEQ ID NO:327	·
`	(i) SEQUENCE CHARACTERISTICS:	
25	(A) LENGTH: 26 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear	
	(ii) MOLECULE TYPE: peptide	
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:327:	
35	Gln Gln Gln Ala Glu Leu Lys Pro Gly L 1 5	ys Gly Thr Pro Gly Gln Gln 10 15
	Asn Lys Asp Lys Ser Ser Thr Ser Glu S 20 25	Ser
40	(328) INFORMATION FOR SEQ ID NO:328	
	(i) SEQUENCE CHARACTERISTICS:	
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear	
•	(ii) MOLECULE TYPE: peptide	
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:328:	

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Glu Gln Gln Ala Glu Leu Arg Ala Gly Lys Gly Ile Pro Gly Gln Glu 1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25

(329) INFORMATION FOR SEQ ID NO:329

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(i) SEQUENCE CHARACTERISTICS: 5 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:329: Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu 15 Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser 20 20 (330) INFORMATION FOR SEQ ID NO:330 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 30 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:330: 35 Gln Gln Gln Ser Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser 40 (331) INFORMATION FOR SEQ ID NO:331 (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 50 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:331:

	1 5 10 15
5	Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser 20 25
10	(332) INFORMATION FOR SEQ ID NO:332
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:332:
	Glu Gln Gln Ala Glu Leu Arg Thr Gly Lys Gly Thr Pro Gly Gln Glu 1 5 10 15
25	Arg Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25
30	(333) INFORMATION FOR SEQ ID NO:333
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:333:
45	Gin Gin Gin Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gin Gin 1 5 10 15
	Lys Lys Asp Lys Ser Ser Thr Phe Glu Ser 20 25
50	(334) INFORMATION FOR SEQ ID NO:334
	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:334:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Thr Gly Ala Pro Gly Gln Glu
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(335) INFORMATION FOR SEQ ID NO:335

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:335:

Gln Gln Gln Pro Glu Val Arg Pro Gly Lys Gly Thr His Ala Lys Gln
1 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25

(336) INFORMATION FOR SEQ ID NO:336

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:336:

Gln Gln Gln Pro Glu Val Arg Pro Gly Lys Asp Thr His Ala Lys Gln
1 5 - 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25

(337) INFORMATION FOR SEQ ID NO:337

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:337: 5 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Glu Gln Glu Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 10 (338) INFORMATION FOR SEQ ID NO:338 (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:338: 25 Glu Gln Gln Thr Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu Lys Lys Gly Arg Ser Ser Thr Ser Glu Ala 30 (339) INFORMATION FOR SEQ ID NO:339. 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:339: 45 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu 1 Lys Lys Ser Lys Pro Ser Thr Ser Glu Ser 50 (340) INFORMATION FOR SEQ ID NO:340 55 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

- (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:340: 5 Gln Gln Gln Ser Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu 10 Lys Lys Ser Lys Pro Ser Thr Ser Glu Ser (341) INFORMATION FOR SEQ ID NO:341 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 20 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:341: 25 Gln Gln Arg Ala Glu Leu Lys Pro Gly Lys Asp Thr Pro Gly Arg Glu 1 30 Lys Lys Asn Lys Pro Ser Thr Ser Glu Ser - 20 (342) INFORMATION FOR SEQ ID NO:342 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid 40 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide . (xi) SEQUENCE DESCRIPTION: SEQ ID NO:342: 45 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu 50 Lys Lys Ser Thr Ser Ser Thr Ser Glu Ser 20

(343) INFORMATION FOR SEQ ID NO:343

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:343: 10 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu 15 Lys Lys Ser Thr Ser Ser Thr Ser Asp Ser 20 15 (344) INFORMATION FOR SEQ ID NO:344 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:344: 30 Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Ile Gln Gln Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser 35 20 (345) INFORMATION FOR SEQ ID NO:345 (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 45 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:345: 50 Gln Gln Gln Ala Glu Phe Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu 10 His Arg Ser Lys Pro Ser Thr Ser Glu Ser 55 (346) INFORMATION FOR SEQ ID NO:346

(i) SEQUENCE CHARACTERISTICS:

. 5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:346:
	Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Ala Leu Gly Gln Glu 1 5 10 15
15	Lys Lys Gly Lys Ser Ser Thr Ser Asp Ser 20 25
20	(347) INFORMATION FOR SEQ ID NO:347
20	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:347:
	Gln Gln Gln Pro Glu Val Lys Pro Gly Lys Gly Ala Pro Gly Lys Gly 1 5 10 15
35	Asn Thr Asp Lys Ser Ser Thr Ser Glu Ser 20 25
. 40	(348) INFORMATION FOR SEQ ID NO:348
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:348:
	Glu Gln Gln Ala Glu Val Arg Ala Gly Lys Gly Ser Pro Gly Gln Glu 1 5 10 15
55	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25

(349) INFORMATION FOR SEQ ID NO:349

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid

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- (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:349:
- Gln Gln Leu Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly His Glu
 1 5 10 15

Lys Lys Gly Ile Ser Ser Thr Ser Glu Ser 20 25

(350) INFORMATION FOR SEQ ID NO:350

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:350:
- Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Lys Pro Glu Gln Glu
 1 5 10 15
 - Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser
 - (351) INFORMATION FOR SEQ ID NO:351
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:351:

1	GIN	GIN	PTO	G10 5	Leu	rys	Pro	GIŸ	Lys Gl	y Arg	Asn ·	Gly I	ys Glu 15	ľ
Asn	Lys	Gly	50 Tàs	Ser	Ser	Thr	Ser	Glu 25	Ser					
(352) INF	FORM	ATION	FOR S	EQ ID	NO:35	2								
(i) SI	EQUE	NCE C	HARAG	CTERIS	STICS:									
((B) TY	NGTH: PE: am POLO	nino aci	id	ds									
(ii) M	OLEC	ULE T	YPE: p	eptide										
(xi) S	SEQUI	ENCE [DESCR	RIPTIOI	N: SEC	ID NO	D:352:							
Gln (Gln	Gln	Thr	Glu 1 5	Leu 1	Arg 1	Pro (Sly A	urg Gly 10	Thr ?	Thr G	ly Gl	n Glu 15	
Arg	Lys	Gly	Lys 20	Ser	Ser	Thr	Ser	Glu 25	Ser			•		
(353) INF	ORM	ATION	FOR S	EQ ID	NO:35	3								
(i) SE	EQUE	NCE C	HARAC	CTERIS	STICS:									
(B) TY	NGTH: PE: am POLO	ino aci	d	ds									
(ii) M	OLĖC	ULE T	YPE: p	eptide										
· (xi) S	SEQUI	ENCE	DESCR	RIPTION	N: SEQ	ID NO	D:353:							
Gln 1	His	Gln	Ala	Glu 5	Leu	Lys	Pro	Gly	Lys Gl 10	y Thr	Pro	Gly I	His Glo	1
Asn	Lys	Val	Thr 20	Ser	Ser	Thr	Ser	Glu 25	Ser			•		
(354) INF	ORM	ATION	FOR S	EQ ID	NO:35	4								
(i) SE	EQUE	NCE CI	HARAC	CTERIS	STICS;									
į (B) TY	NGTH: PE: am POLO	ino aci	d	is									
(ii) M	OLEC	ULE T	YPE: pe	eptide										

(xi) SEQUENCE	DESCRIPTION:	SEQ ID	NO:354:
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Glu Gln Gln Ala Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu 1 5 10 15

Gln Lys Ala Lys Ser Ser Thr Ser Glu Ser

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(355) INFORMATION FOR SEQ ID NO:355

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:355:

Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln 1 5 10 15

Lys Thr Gly Thr Ser Ser Thr Thr Glu Ser 20 25

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(356) INFORMATION FOR SEQ ID NO:356

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:356:

Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Asn Pro Gly Gln Glu
1 5 10 15

Lys Lys Ser Thr Ser Ser Ala Ser Glu Ser 20 25

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(357) INFORMATION FOR SEQ ID NO:357

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:357: 5 Glu Gln Gln Thr Val Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Gln Lys Lys Gly Thr Ser Ala Thr Asn Glu Ser 10 (358) INFORMATION FOR SEQ ID NO:358 (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:358: 25 Gin Gin Leu Thr Glu Leu Lys Pro Gly Asn Gly Thr Pro Gly Gin Glu 10 Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser 30 (359) INFORMATION FOR SEQ ID NO:359 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:359: 45 Gln Gln Gln Ser Val Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Glu 1 Lys Lys Gly Thr Ser Ser Thr Ser Lys Ser 20 (360) INFORMATION FOR SEQ ID NO:360 55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear

5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:360:
10	Leu Gln Gln Pro Val Leu Lys Pro Gly Lys Gly Ser His Gly Lys Gln 1 5 10 15
	Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser 20 25
15	(361) INFORMATION FOR SEQ ID NO:361
	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:361:
30	Glu Gln Gln Pro Glu Thr Lys Pro Gly Lys Gly Thr Leu Gly Lys Gln 1 5 10 15
	Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser 20 25
35	(362) INFORMATION FOR SEQ ID NO:362
	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:362:
50	Gln Gln Gln Ala Glu Leu Lys Pro Gly Gln Gly Thr Pro Gly Gln Glu 1 5 10 15
55	Lys Lys Asn Lys Ser Ser Thr Pro Glu Phe 20 25
	(363) INFORMATION FOR SEQ ID NO:363

	(i) SEQUENCE CHARACTERISTICS:
5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:363:
10	
	Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Asn Pro Glu Gln Pro 1 5 10 15
15	Lys Gln Gly Thr Ser Ser Thr Ser Glu Thr 20 25
20	(364) INFORMATION FOR SEQ ID NO:364
20	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:364:
	Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Asn Pro Glu Gln Pro 1 5 10 15
35	Lys Gln Gly Thr Ser Thr Thr Ser Glu Thr 20 25
	(365) INFORMATION FOR SEQ ID NO:365
40	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:365:
	Glu Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Asn Pro Glu Gln Pro 1 5 10 15
55	Lys Gln Gly Thr Ser Ser Thr Ser Glu Thr

(366) INFORMATION FOR SEQ ID NO:366 (i) SEQUENCE CHARACTERISTICS: 5 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:366: Glu Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Asn Pro Glu Gln Pro 15 Lys Gln Asp Thr Ser Ser Thr Ser Glu Thr 20 (367) INFORMATION FOR SEQ ID NO:367 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:367: Glu Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Asn Pro Glu Gln Pro 35 Lys Gln Gly Thr Ser Ser Thr Ser Gly Thr 20 40 (368) INFORMATION FOR SEQ ID NO:368 (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:368:

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Glu Gln Gln Ala Glu Val Lys Pro Gly Lys Gly Asn Pro Glu Gln Pro 1 5 10 15

5	Lys Gln Gly Thr Ser Ser Thr Ser Glu Thr 20 25
10	(369) INFORMATION FOR SEQ ID NO:369
	(i) SEQUENCE CHARACTERISTICS:
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:369:
	Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Asn Pro Glu Gln Pro 1 5 10 15
25	Lys Gln Val Thr Ser Ser Thr Ser Glu Thr 20 25
30	(370) INFORMATION FOR SEQ ID NO:370
	(i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:370:
	Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Asn Pro Glu Gln Pro 1 5 10 15
45	Lys Gln Ile Thr Ser Ser Thr Ser Glu Thr 20 25
50	(371) INFORMATION FOR SEQ ID NO:371
	(i) SEQUENCE CHARACTERISTICS:
55	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide

	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:371:							
5	Glu Gln Gln Ala Glu Leu Arg Pro Gly Arg Gly Asn Pro Glu Gln Pro 1 5 10 15							
	Lys Gln Val Thr Ser Ser Thr Ser Glu Thr 20 25							
10	(372) INFORMATION FOR SEQ ID NO:372							
	(i) SEQUENCE CHARACTERISTICS:							
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear							
20	(ii) MOLECULE TYPE: peptide							
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:372:							
25	Glu Gln Gln Ala Glu Leu Arg Pro Gly Arg Gly Asn Pro Glu Gln Pro 1 5 10 15							
	Lys His Val Thr Ser Ser Thr Ser Glu Thr 20 25							
30	(373) INFORMATION FOR SEQ ID NO:373							
	(i) SEQUENCE CHARACTERISTICS:							
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear							
40	(ii) MOLECULE TYPE: peptide							
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:373:							
45	Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Asn Thr Glu Gln Pro 1 5 10 15							
	Lys Gln Val Thr Ser Ser Thr Ser Glu Thr 20 25							
50	(374) INFORMATION FOR SEQ ID NO:374							

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:374:
5	Glu Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Asn Thr Glu Gln Pr 1 5 10 15
0	Lys Leu Ile Thr Ser Ser Thr Ser Glu Thr 20 25
	(375) INFORMATION FOR SEQ ID NO:375
5	(i) SEQUENCE CHARACTERISTICS:
0	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:375:
25	Thr Gly Gln Ala Glu Leu Arg Pro Gly Lys Gly Ala Pro Glu Gln Gl 1 5 10 15
80	Lys Lys Gly Lys Ser Ser Thr Ser Asp Arg 20 25
	(376) INFORMATION FOR SEQ ID NO:376
35	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
0	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:376:
:5	
	Gln Tyr Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Arg Gln Gln 1 5 10 15
ю	Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser 20 25
	(377) INFORMATION FOR SEQ ID NO:377
5	(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:377: Gln Gln Gln Ala Val Leu Arg His Gly Lys Gly Thr His Gly Gln Glu 10 Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser (378) INFORMATION FOR SEQ ID NO:378 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 20 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:378: Gin Gin Thr Lys Leu Gly Pro Gly Arg Gly Thr Pro Gly Gin Gly 30 Arg Lys Gly Lys Ser Ser Thr Ser Gly Ser 20 (379) INFORMATION FOR SEQ ID NO:379 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 40 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:379: Glu Gln Gln Ala Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu 1 10 50 Lys Lys Gly Lys Ser Ser Val Tyr Phe Ala 20 25

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(380) INFORMATION FOR SEQ ID NO:380

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids(B) TYPE: amino acid(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:380: Glu Gln Gln Ala Glu Leu Lys Ala Gly Lys Gly Thr Pro Gly Gln Gln 10 Lys Gln Gly Glu Ser Thr Arg Ser Glu Thr 15 (381) INFORMATION FOR SEQ ID NO:381 (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 25 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:381: Gln Gln Lys Ala Glu Leu Ala Ala Ser Lys Gly Thr Pro Gly Gln Glu 30 Lys Lys Gly Arg Ser Ser Thr Ser Glu Ser 35 (382) INFORMATION FOR SEQ ID NO:382 (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 45 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:382: Gln Gln Gln Thr Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Glu 50 5 Lys Arg Gly Lys Ser Ser Asn Leu Arg Leu 20 55 (383) INFORMATION FOR SEQ ID NO:383

(i) SEQUENCE CHARACTERISTICS:

5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:383:
	Glu Lys Val Gly Gly Leu Gln Gly Ser Ser Phe Asp Pro Gly Lys Ala
15	Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr 20 25
20	(384) INFORMATION FOR SEQ ID NO:384
	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:384:
35	Glu Gln Gln Ala Asp Leu Lys Leu Gly Lys Gly Asn Pro Glu Gln Pro 1 5 10 15
33	Lys Leu Ala Thr Pro Ser Thr Ser Glu Thr 20 25
40	(385) INFORMATION FOR SEQ ID NO:385
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:385:
55	Glu Gln Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Asp Lys Ser 1 5 10 15 Asp Val Lys Asp Asn Ala Lys Ser Glu Thr
	20 25

(386) INFORMATION FOR SEQ ID NO:386

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(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 5 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:386: Asp Gln Gln Pro Asp Leu Lys Pro Ser Ser Gly Ser Pro Gly His Pro Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr 20 25 20 (387) INFORMATION FOR SEQ ID NO:387 (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:387: Asp Gln Gln Pro Asp Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 35 Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr 40 (388) INFORMATION FOR SEQ ID NO:388 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 45 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:388:

	Asp Gln Gln Pro Asp Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 1 5 10 15
5	Ser Lys Ser Thr Ser Lys Thr Ala Glu Thr 20 25
o	(389) INFORMATION FOR SEQ ID NO:389 (i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid
5	(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:389:
	Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 1 5 10 15
25	Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr 20 25
80	(390) INFORMATION FOR SEQ ID NO:390 (i) SEQUENCE CHARACTERISTICS:
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:390:
	Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 1 5 10 15
15	Ser Lys Asn Thr Ser Lys Thr Thr Glu Thr 20 25
50	(391) INFORMATION FOR SEQ ID NO:391 (i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid
55	(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:391:

Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asp Pro 1 5 10 15

Ser Lys Thr Thr Ser Lys Thr Thr Glu Thr 20 · 25

(392) INFORMATION FOR SEQ ID NO:392

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:392:
- Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
 1 5 10 15

Ser Lys Thr Thr Ser Lys Thr Thr Glu Thr 20 25 .

(393) INFORMATION FOR SEQ ID NO:393

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:393:
- Asp His Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 1 5 10 15

Ser Lys Asn Thr Ser Lys Thr Thr Glu Thr 20 25

(394) INFORMATION FOR SEQ ID NO:394

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:394: 5 Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro Ser Arg Ser Thr Ser Lys Thr Thr Glu Thr 10 20 (395) INFORMATION FOR SEQ ID NO:395 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 20 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:395: 25 Asp Gln Gln Pro Gly Leu Lys Pro Ser Ala Gly Ser Pro Gly Asn Pro Ser Lys Ser Thr Ser Lys Thr Ala Glu Thr 30 20 (396) INFORMATION FOR SEQ ID NO:396 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear 40 (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:396: 45 Glu Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 15 Ser Lys Ser Thr Ser Lys Thr Ser Glu Thr 50 20 (397) INFORMATION FOR SEQ ID NO:397 55 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

(C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:397: 5 Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 10 Ser Lys Asn Thr Ser Lys Thr Ile Glu Thr (398) INFORMATION FOR SEQ ID NO:398 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid 20 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:398: 25 Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asp Pro . 30 Ser Lys Asn Thr Ser Lys Thr Pro Glu Thr 35 (399) INFORMATION FOR SEQ ID NO:399 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids (B) TYPE: amino acid 40 (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide (xi) SEQUENCE DESCRIPTION: SEQ ID NO:399: 45 Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 50 Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr 25 20

177

(400) INFORMATION FOR SEQ ID NO:400

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear

5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:400:
10	Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 1 5 10 15
15	Ser Lys Asn Thr Ser Glu Thr Thr Glu Thr 20 25
	(401) INFORMATION FOR SEQ ID NO:401
20	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:401:
30	Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 1 5 10 15
35	Ser Lys Asn Thr Ser Glu Thr Thr Glx Thr 20 25
	(402) INFORMATION FOR SEQ ID NO:402
40	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:402:
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	Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 1 10 15
55	Ser Lys Ser Thr Ser Lys Thr Ser Glu Thr 20 25
	(403) INFORMATION FOR SEQ ID NO:403

	(I) SEQUENCE CHARACTERISTICS.
5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:403:
	Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 1 5 10 15
15	Ser Lys Ser Thr Ser Arg Thr Thr Glu Thr 20 25
20	(404) INFORMATION FOR SEQ ID NO:404
20	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:404:
	Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 1 5 10 15
· 35	Ser Lys Ser Thr Ser Lys Thr Ala Glu Thr 20 25
40	(405) INFORMATION FOR SEQ ID NO:405
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:405:
55	Asp Gln Gln Pro Asp Leu Lys Pro Ser Ser Gly Phe Pro Gly Asn Pro 1 5 10 15
	Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr

(406) INFORMATION FOR SEQ ID NO:406 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 5 (B) TYPE: amino acid · (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:406: Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Lys Pro 15 Ser Lys Ser Thr Ser Lys Thr Asn Glu Thr 20 (407) INFORMATION FOR SEQ ID NO:407 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 26 amino acids 25 (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:407: Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 35 Ser Lys Ser Thr Phe Lys Thr Ser Glu Thr 20 40 (408) INFORMATION FOR SEQ ID NO:408 (i) SEQUENCE CHARACTERISTICS: 45 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear (ii) MOLECULE TYPE: peptide

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:408:

	Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 1 10 15					
5	Ser Lys Ser Thr Ser Thr Thr Ser Glu Thr 20 25					
10	(409) INFORMATION FOR SEQ ID NO:409 (i) SEQUENCE CHARACTERISTICS:					
15	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear					
	(ii) MOLECULE TYPE: peptide					
20	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:409:					
	Glu Gln Gln Leu Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro 1 10 15					
25	Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr					
	(410) INFORMATION FOR SEQ ID NO:410					
30	(i) SEQUENCE CHARACTERISTICS:					
35	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear					
	(ii) MOLECULE TYPE: peptide					
40	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:410:					
	Gln Gln Gln Pro Gly Leu Lys Pro Ser Phe Gly Pro Pro Gly Lys Pro 1 10 15					
45	Ser Gln Ser Thr Ser Lys Thr Thr Glu Thr 20 25					
50	(411) INFORMATION FOR SEQ ID NO:411					
	(i) SEQUENCE CHARACTERISTICS:					
55	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear					
	(ii) MOLECULE TYPE: popula					

(xi)	SEQUE	ENCE (DESCRIP	MOIT	SEQI) NO:411:

Gln Gln Lys Pro Gly Leu Ala Pro Ser Ser Gly Ser Pro Gly Lys Ser 1 5 10 15

Thr Lys Ser Asn Ser Lys Gln Thr Asp Thr 20 25

(412) INFORMATION FOR SEQ ID NO:412

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:412:
- Gln Gln Lys Pro Gly Leu Ala Pro Ser Ser Gly Ser Pro Gly Lys Ser
 - Ala Lys Ser Asn Ser Lys Gln Thr Asp Thr
 - (413) INFORMATION FOR SEQ ID NO:413
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:413:
- Gln Gln Lys Pro Gly Leu Ala Pro Ser Ser Gly Ser Pro Gly Lys Ser

 1 10 15
 - Ala Met Ser Asn Ser Lys Gln Thr Asp Thr 20 25
 - (414) INFORMATION FOR SEQ ID NO:414
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 26 amino acids
 - (B) TYPE: amino acid
 - (C) TOPOLOGY: linear

	(II) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:414:
5	Gln Gln Lys Pro Gly Leu Ala Pro Ser Ser Gly Ser Pro Gly Lys Ser 1 5 10 15
10	Ala Ile Ser Asn Ser Lys Gln Thr Asp Thr 20 25
	(415) INFORMATION FOR SEQ ID NO:415
15	(i) SEQUENCE CHARACTERISTICS:
. 20	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
20	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:415:
25	Gln Gln Lys Pro Gly Leu Gln Pro Ser Ser Gly Ser Pro Gly Lys Ala 1 5 10 15
30	Ala Ile Ser Asn Ser Lys Gln Ser Asn Thr 20 25
	(416) INFORMATION FOR SEQ ID NO:416
35	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:416:
45	Gln Gln Lys Pro Gly Leu Gln Pro Ser Ser Gly Ser Pro Gly Lys Ala 1 5 10 15
50	Ala Ile Ser Asn Ser Lys Gln Ala Asn Thr 20 25
55	(417) INFORMATION FOR SEQ ID NO:417
55	(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid (C) TOPOLOGY: linear

5	(ii) MOLECULE TYPE: peptide
J	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:417:
10	Gln Gln Lys Pro Val Leu Ala Pro Ser Ser Gly Ser Pro Gly Lys Ser 1 5 10 15
	Ala Met Ser Asn Ser Lys Gln Ile Asp Thr 20 25
15	(418) INFORMATION FOR SEQ ID NO:418
	(i) SEQUENCE CHARACTERISTICS:
20	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
25	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:418:
30	Gln Gln Lys Pro Ser Leu Gln Pro Ser Ser Asp Ser Pro Gly Lys Ala 1 5 10 15
	Ala Met Ser Asn Ser Lys Gln Ala Asp Thr 20 25
35	(419) INFORMATION FOR SEQ ID NO:419
	(i) SEQUENCE CHARACTERISTICS:
40	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
45	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:419:
50	Glu Arg Val Gly Asp Leu Glu Pro Gly Arg Gly Ile Pro Gly Lys Ala 1 5 10 15
	Pro Lys Gly Asp Ser Lys Lys Ile Glu Thr 20 25
55	(420) INFORMATION FOR SEQ ID NO:420
	(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids (B) TYPE: amino acid

	(C) TOPOLOGY: linear
5	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:420:
10	Glu Arg Val Gly Asp Leu Glu Pro Glu Arg Gly Ile Pro Gly Lys Ala 1 5 10 15
15	Pro Lys Gly Asp Ser Lys Lys Ile Glu Thr 20 25
	(421) INFORMATION FOR SEQ ID NO:421
20	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
25	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:421:
30	Glu Gln Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Gly Lys Ala 1 5 10 15
35	Pro Lys Gly Asp Ser Lys Lys Thr Glu Thr 20 25
•	(422) INFORMATION FOR SEQ ID NO:422
40	(i) SEQUENCE CHARACTERISTICS:
	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
45	(ii) MOLECULE TYPE: peptide
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:422:
50	Glu Gln Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Ser Gly Lys Ala 1 5 10 15
55	Ser Lys Gly Asp Ser Lys Lys Thr Glu Thr
	(423) INFORMATION FOR SEQ ID NO:423

(i) SEQUENCE CHARACTERISTICS:

5	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
10	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:423:
	Glu Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asx 1 5 10 15
15	Ser Lys Gly Asp Ser Lys Arg Ala Glu Thr 20 25
20	(424) INFORMATION FOR SEQ ID NO:424
	(i) SEQUENCE CHARACTERISTICS:
25	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	· (ii) MOLECULE TYPE: peptide
30	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:424:
	Glu Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp 1 10 15
35	Ser Lys Gly Asn Ser Lys Arg Ala Glu Thr 20 25
40	(425) INFORMATION FOR SEQ ID NO:425
	(i) SEQUENCE CHARACTERISTICS:
45	(A) LENGTH: 26 amino acids (B) TYPE: amino acid (C) TOPOLOGY: linear
	(ii) MOLECULE TYPE: peptide
50	(xi) SEQUENCE DESCRIPTION: SEQ ID NO:425:
	Glu Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp 1 5 10 15
55	Ser Arg Gly Asn Ser Lys Arg Ala Glu Thr 20 25